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ALTERNATING CURRENT POLAROGRAPHY OF ORGANIC COMPOUNDS

II. QUINONE AND HYDROQUINONE

By B. Breyer* and H. H. Bauer*

[*Manuscript received April* 12, 1955]

Summary

The alternating current polarography of quinone and hydroquinone has been investigated. The calibration curves follow an equation of the type of the Langmuir isotherm. The method can be used for quantitative analysis, the accuracy being greatest at low temperatures and in a concentration range between 10^{-5} and 10^{-4}M.

I. Introduction

It has been shown by numerous workers (Müller and Baumberger 1937; Müller 1939, 1940; Kolthoff and Orlemann 1941; Smith *et al.* 1941) that the quinone-hydroquinone system can be reduced or oxidized reversibly at the dropping mercury electrode. The process involves the transfer of two electrons.

The present paper considers results obtained in an A.C. polarographic study of this system.

II. Experimental

Conventional polarograms were obtained by means of a manual-type polarograph. For A.C. polarography, the apparatus described by Breyer, Gutmann, and Hacobian (1950, 1953) was used. The superposed alternating voltage had an amplitude of 15 mV r.m.s. and a frequency of 50 c/s.

Experiments were performed in Prideaux and Ward "Universal" buffers (Prideaux and Ward 1924) of pH 7·3 and 9·0. The capillary characteristics were $m=0{\cdot}83$ mg/sec, $t=6{\cdot}8$ sec (at zero applied potential) at a mercury reservoir height of 76·5 cm.

Quinone was freshly resublimed before each experiment; the samples of hydroquinone and quinhydrone used were recrystallized commercial preparations. Fresh solutions were prepared daily.

III. Results

(*a*) *D.C. Polarography*

The salient features of the results were:

(i) The slope of the log $(i_d-i)/i$ *v.* E plot was the same whether quinone, hydroquinone, or quinhydrone was used. The values found were 30·4 mV at pH 7·3 and 40·4 mV at pH 9·0.

* Physico-Chemical Laboratories, Faculty of Agriculture, University of Sydney.

(ii) The Ilkovič constant was not the same for the different forms. Thus, for instance, at pH 7·3 it was $5{\cdot}3\times10^3$ μA l. mole^{-1} for quinhydrone and $6{\cdot}5\times10^3$ for hydroquinone; at pH 9·0, $7{\cdot}2\times10^3$ for quinone and $3{\cdot}7\times10^3$ for hydroquinone. This fact was first observed by Smith *et al.* (1941), who ascribed it to differences in the diffusion coefficients of the various species.

(iii) The height of the step varied as the square root of the height of the mercury reservoir (Table 1), indicating a diffusion-controlled reduction process.

TABLE 1

VARIATION OF A.C. AND D.C. CURRENTS WITH HEIGHT OF MERCURY VESSEL

Concentration (M)	Diffusion Current (μA)			Alternating Current (μA)		
	$H=76{\cdot}5$ (cm) (i)	$H=44{\cdot}5$ (cm) (ii)	(i)/(ii)	$H=76{\cdot}5$ (cm) (iii)	$H=44{\cdot}5$ (cm) (iv)	(iii)/(iv)
Quinone						
$8{\cdot}5\times10^{-5}$ ..	0·395	0·301	1·31	7·0	7·0	1·00
$2{\cdot}9\times10^{-4}$ ..	1·64	$1{\cdot}28_5$	1·28	15·2	14·8	1·03
$7{\cdot}7_5$ ..	4·44	3·32	1·34	20·1	19·9	1·01
$1{\cdot}4\times10^{-3}$ ..	7·8	6·15	1·27	21·8	21·6	1·01
4·3 ..	24·9	18·5	1·35	24·9	24·9	1·00
Hydroquinone						
$1{\cdot}3\times10^{-4}$ ..	0·61	$0{\cdot}44_5$	1·37	8·25	8·8	0·94
4·3 ..	1·78	1·17	1·52	17·0	16·7	1·02
$1{\cdot}1\times10^{-3}$ ..	4·2	2·94	1·43	20·0	20·5	0·98
$1{\cdot}9_5$ ..	7·0	4·9	1·43	22·0	22·0	1·00
$4{\cdot}7_5$ ..	17·0	4·2	1·52	23·0	23·8	0·97
Mean			1·38	$\sqrt{(H_1/H_2)}=1{\cdot}31$		$0{\cdot}99_5$

(*b*) *A.C. Polarography*

(i) The alternating current was found to be independent of the height of the mercury reservoir (Table 1). This result is predicted by equation (**41**) of Breyer and Hacobian's (1954) paper in which it was shown that the alternating current is linearly proportional to the term $(mt)^{\frac{1}{2}}$, a quantity which is independent of the height of the mercury column.

(ii) The calibration curves were markedly non-linear. They can be described by the equation

$$i_{\sim(E_s)}=\frac{abC}{1+bC},$$

where $i_{\sim(E_s)}$ is the alternating current at the summit potential, C the bulk concentration of depolarizer, and a and b are adjustable parameters. The best values of a and b are the same for quinone, hydroquinone, and quinhydrone, and are also the same at the two pH values of 7·3 and 9·0. At 3 °C, $a=15{\cdot}7$ μA

and $b=1\cdot45\times10^{4}$ l. mole^{-1}; at 20 °C, $a=22\cdot9$ μA and $b=4\cdot2\times10^{3}$ l. mole^{-1}. The fit of the experimental points to these equations is shown in Figures 1 and 2.

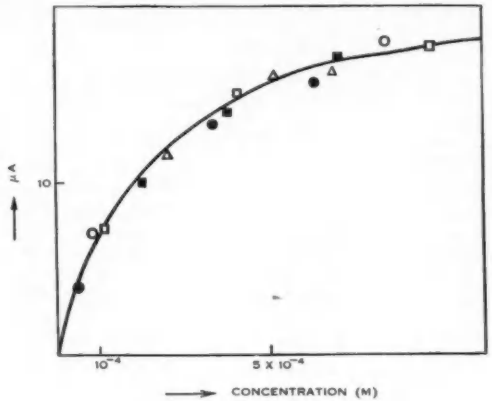

Fig. 1.—Calibration curve, 20 °C.
—— Curve of best fit (see text). ○ Quinone, pH 7·3.
□ Quinhydrone, pH 7·3. △ Hydroquinone, pH 7·3.
● Quinone, pH 9·0. ■ Hydroquinone, pH 9·0.

(iii) The effect of temperature on the height of the wave varies with concentration of the substances, as shown in Table 2.

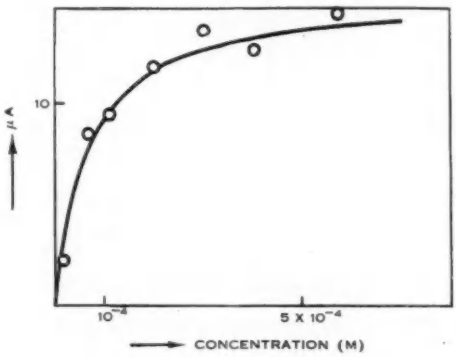

Fig. 2.—Calibration curve, 3 °C.
—— Curve of best fit (see text). ○ Hydroquinone, pH 9·0.

(iv) At higher concentrations of depolarizer, the height of the wave tended to a limiting value and the wave became broader (Fig. 3). This phenomenon is under investigation at present.

IV. Conclusions

The results obtained are typical for organic compounds. As already discussed in Part I of this series (Breyer, Bauer, and Hacobian 1954) the non-linearity of the calibration curves can be explained in terms of adsorption processes.

Table 2

VARIATION OF A.C. CURRENT WITH TEMPERATURE

Concentration (M)	Alternating Current (μA)		
	3 °C (i)	20 °C (ii)	(i)/(ii)
5×10^{-5}	6·6	4·0	1·65
1×10^{-4}	9·3	6·8	1·37
3	12·8	$12\cdot7_5$	$1\cdot00_5$
6	14·1	16·4	0·86
1×10^{-3}	14·7	18·5	$0\cdot79_5$

The fact that the height and shape of the A.C. wave remain unaltered at pH 7·3 and at pH 9·0, while the log-plot slope of the D.C. polarogram changes from 30·4 to 40·4 mV, demonstrates once again the fact that the A.C. and D.C.

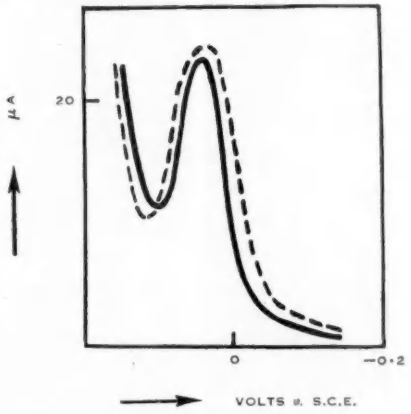

Fig. 3.—A.C. polarographic waves of quinone, pH 7·3.

—— $7\cdot4\times10^{-4}$M. ---- $1\cdot1\times10^{-3}$M.

polarographic processes are fundamentally different. Details of these differences will be found elsewhere (Breyer, Bauer, and Hacobian 1954, 1955).

A.C. polarography can be used for quantitative estimation of quinone, hydroquinone, and quinhydrone, but the accuracy falls off rapidly at concentrations higher than 10^{-4}M, when the height of the wave varies but little

with concentration. At concentrations between 10^{-5} and 10^{-4}M the substances can be estimated with an accuracy comparable to that in any polarographic work. The sensitivity of the method increases at lower temperatures (cf. Table 2) because of increasing adsorption of the substances at the electrode.

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ALTERNATING CURRENT POLAROGRAPHY OF ORGANIC COMPOUNDS

III. CHLORANILIC ACID

By B. BREYER* and H. H. BAUER*

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Summary

The behaviour of chloranilic acid at the dropping mercury electrode has been investigated by the techniques of ordinary and of alternating current polarography. A new type of tensammetric wave has been encountered, which is probably an outcome either of multilayer adsorption and/or of a change in state of the adsorbed film. At the same time, a new tensammetric phenomenon, the exchange of one species of surface-active molecules against another, has been observed.

Alternating current polarography can be used for estimating chloranilic acid at concentrations as low as 10^{-7}M, whereas conventional polarography does not permit analysis at concentrations below 10^{-5}M.

I. INTRODUCTION

It is the purpose of the present paper to report experimental results obtained with D.C. and A.C. polarography of chloranilic acid. The relationship between alternating current and concentration is non-linear, as found with all other organic substances investigated (Breyer 1953; Breyer, Bauer, and Hacobian 1954). The theory underlying this phenomenon will be discussed in detail in Part V of this series.

At higher concentrations of chloranilic acid, a small tensammetric step appears at a potential of about $-0{\cdot}1$ V *versus* the saturated calomel electrode. The lowering of the base current on both sides of the tensammetric step indicates that organic molecules are adsorbed in both regions of potential. The step is, therefore, due to some rearrangement of the adsorbed film, such as a change in its structure or in the number of adsorbed layers.

In the presence of *cyclo*hexanol, the A.C. polarographic wave of chloranilic acid disappears and the tensammetric wave of *cyclo*hexanol is shifted to more negative potentials, indicating a probable displacement of one molecular species by the other within a certain range of potential.

A.C. waves of chloranilic acid are observed at very low concentrations, allowing determination of the substance at concentrations down to 10^{-7}M. This high sensitivity is probably due to the great adsorbability of chloranilic acid onto the electrode.

II. EXPERIMENTAL

The apparatus used, including D.C. and A.C. polarographs, thermostat, capillary, and buffer composition, were the same as those described in Part II of this series (Breyer and Bauer 1955). The alternating voltage was 15 mV

* Physico-Chemical Laboratories, Faculty of Agriculture, University of Sydney.

r.m.s., the frequency 50 c/s. The capillary characteristics were $m=0\cdot83$ mg/sec, $t=6\cdot8$ sec. Prideaux and Ward " Universal " buffer (Prideaux and Ward 1924) was used throughout.

Chloranilic acid was prepared and purified following the method of Graebe (1891).

III. Results

(*a*) *D.C.Polarography*

The calibration curves at all pH values investigated were linear; the Ilkovič constant was the same, within experimental error, at pH values of 4·9, 7·1, 9·0, and 12·0, but greater at pH 2·2 (Table 1).

Table 1

Effect of pH change on the half-step potential and the Ilkovič constant of chloranilic acid

pH	$E_{\frac{1}{2}}$ (V *v.* S.C.E.)	Ilkovič Constant (μA l. mole^{-1})
2·2	——*	$7\cdot25\times10^3$
4·9	—0·31	$4\cdot45\times10^3$
7·1	—0·47	$4\cdot25\times10^3$
9·0	—0·62	$4\cdot6\times10^3$
12·0	—0·82; —0·95	$4\cdot3\times10^3$†

* Changes from —0·02 at 10^{-5}M to +0·03 at 10^{-3}M.
† Combined prestep and main step.

The half-step potentials were practically independent of concentration, except at pH 2·2; in the latter case the polarograms actually consisted of two

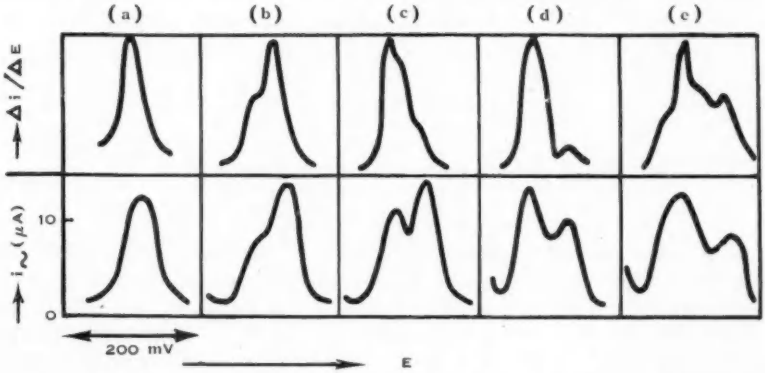

Fig. 1.—Derivative polarograms (upper curves) and A.C. polarograms (lower curves) of chloranilic acid in Prideaux and Ward buffer pH 2·2. Air-free solutions. Chloranilic acid concentration: (*a*) $1\cdot2\times10^{-5}$M; (*b*) $4\cdot6\times10^{-5}$M; (*c*) $1\cdot7\times10^{-4}$M; (*d*) $6\cdot3\times10^{-4}$M; (*e*) $1\cdot2\times10^{-3}$M.

steps very close together, as shown by the derivative curves of the D.C. polarograms (Fig. 1).

At pH 12·0, a small prestep was observed, the height of which reached a constant value with increasing concentration.

The slope of the log $(i_d - i)/i$ *v.* E plot was 35 mV at pH 4·9, 32 mV at pH 7·1, and 38 mV at pH 9·0. The plot was non-linear at pH 12·0 and also at pH 2·2, in the latter case because the polarogram consisted of two steps too close together, as already mentioned.

In the presence of *cyclo*hexanol, which forms a film at the surface of the electrode, the steps were flatter and shifted towards more negative potentials, but were unchanged in height.

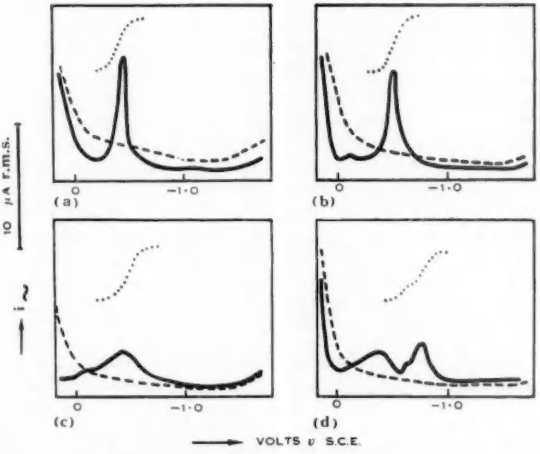

Fig. 2.—A.C. and D.C. polarograms of chloranilic acid in Prideaux and Ward buffer. Air-free solutions.

···· D.C. polarogram.
—— A.C. polarogram.
---- A.C. base current.
(*a*) pH 4·9; (*b*) pH 7·1; (*c*) pH 9·0; (*d*) pH 12·0.

(*b*) *A.C. Polarography*

At pH 2·2, two A.C. waves were observed at concentrations above 3×10^{-5}M; there was a similarity between the A.C. polarograms and the derivative curves of the D.C. steps (Fig. 1). At pH 4·9 (Fig. 2 (*a*)) and at pH 7·1 (Fig. 2 (*b*)) single well-defined A.C. waves were observed. At pH 9·0 (Fig. 2 (*c*)) only an ill-defined " hump ", spreading over a potential range of about 0·4 V, could be distinguished. At pH 12·0 (Fig. 2 (*d*)), two small waves were observed (corresponding to the two D.C. steps) together with a broad " hump ".

The base current of the supporting electrolyte was lowered in the presence of chloranilic acid (Fig. 3); in addition, there was a slight rise in current at negative potentials (at pH 4·9; wave *X*, Fig. 3 (*a*)). The lowering of the base current increased with increasing concentration of chloranilic acid; however,

above a certain concentration, the base current was lowered further only at potentials more positive than a potential E_1 (Fig. 3) and not over the whole range of potentials where adsorption had already occurred.

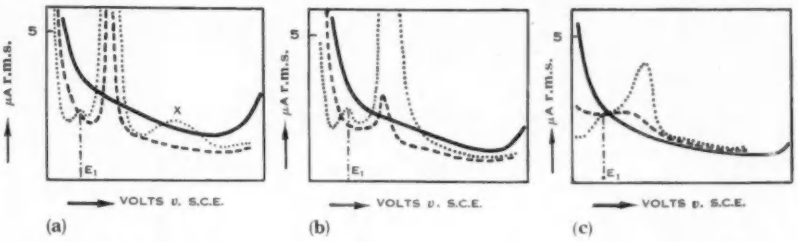

Fig. 3.—Effect of chloranilic acid on the A.C. base current in Prideaux and Ward buffer. Air-free solutions.

—— Buffer alone.
---- 10^{-5}M chloranilic acid added.
···· 10^{-3}M chloranilic acid added.
(*a*) pH 4·9; (*b*) pH 7·1; (*c*) pH 9·0.

The calibration curves were markedly non-linear (see Fig. 4); they fitted the empirical equation

$$i_{\sim(E_s)}=\frac{abc}{1+bc}\cdot\left(1+\frac{\alpha\beta c}{1+\beta c}\right), \quad \ldots\ldots\ldots\ldots \quad (1)$$

where $i_{\sim(E_s)}$ is the alternating current at the summit potential, C the bulk concentration of chloranilic acid, and a, b, α, β are adjustable parameters whose values are given in Table 2.

TABLE 2

PARAMETERS DESCRIBING THE A.C. POLAROGRAPHIC CALIBRATION CURVES OF CHLORANILIC ACID

pH	Temp. (°C)	a (μA)	b (l. mole^{-1})	α	β (l. mole^{-1})
2·2*	20	26·9	$7{\cdot}4\times10^4$	—0·50	$3{\cdot}1\times10^4$
	3	18·8	$6{\cdot}5\times10^4$	—0·47	$3{\cdot}0\times10^4$
2·2†	20	24·2	$4{\cdot}6\times10^3$	0	—
	3	14·05	$2{\cdot}1\times10^4$	0	—
4·9	20	27·6	$6{\cdot}1\times10^4$	$-0{\cdot}66_5$	$4{\cdot}5\times10^4$
	3	12·6	$7{\cdot}4\times10^4$	—0·50	$3{\cdot}3\times10^4$
7·1	20	7·45	$3{\cdot}7\times10^4$	$0{\cdot}44_5$	$4{\cdot}2\times10^4$
	3	5·55	$7{\cdot}8\times10^4$	0	—

* First wave.
† Second wave.

As in the case of quinone (cf. Part II of this series, Breyer and Bauer 1955) the effect of temperature on the height of the A.C. wave varied with concentration (Table 3).

In the presence of *cyclo*hexanol, the A.C. waves of chloranilic acid disappeared. The tensammetric waves (cf. Breyer and Hacobian 1952) of *cyclo*-

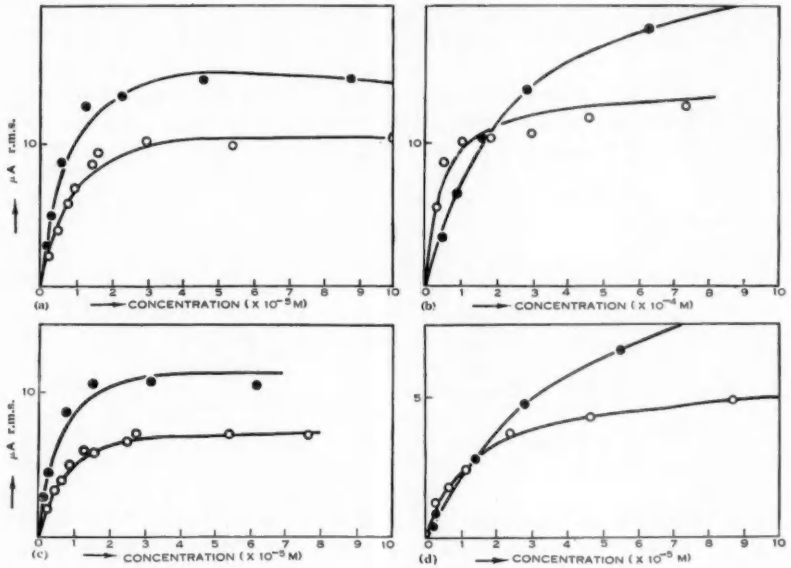

Fig. 4.—A.C. polarographic calibration curves of chloranilic acid in Prideaux and Ward buffer. Air-free solutions.

○ Experimental points at 3 °C.
● Experimental points at 20 °C.
—— Curves calculated from equation (1).
(*a*) pH 2·2; first wave; (*b*) pH 2·2, second wave; (*c*) pH 4·9; (*d*) pH 7·1.

hexanol were still present, but were shifted; with increasing concentration of chloranilic acid, the positive tensammetric wave shifted to more negative

TABLE 3
EFFECT OF TEMPERATURE CHANGE ON THE A.C. POLAROGRAPHIC PEAK CURRENT

Concentration (M)	Values of $i_{\sim(E_s)}$ 3 °C/$i_{\sim(E_s)}$ 20 °C			
	pH 2·2*	pH 2·2†	pH 4·9	pH 7·1
10^{-6}	0·62	2·65	0·56	1·48
10^{-5}	0·66	2·42	0·57	1·07
10^{-4}	0·72	1·24	0·64	0·62
10^{-3}	0·74	0·68	0·68	0·53

* First wave.
† Second wave.

potentials, and first decreased and then increased in height; the negative wave was also shifted to more negative potentials, but its height was little affected (Fig. 5). These effects were qualitatively the same at all pH values investigated (4·9, 7·1, 9·0, and 12·0) and for concentrations of *cyclo*hexanol between 0·05 and 0·15M.

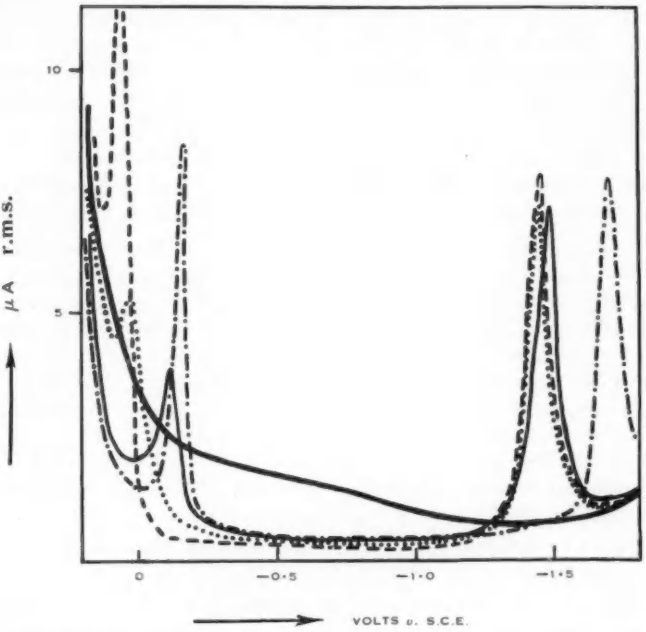

Fig. 5.—Effect of chloranilic acid on the tensammetric waves of *cyclo*hexanol in Prideaux and Ward buffer pH 4·9. Air-free solutions.

—— Buffer alone.
---- 0·15M *cyclo*hexanol added.
···· As above+10^{-6}M chloranilic acid.
—— As above+10^{-5}M chloranilic acid.
–·–· As above+10^{-4}M chloranilic acid.

IV. Discussion

(*a*) *Nature and Height of the Polarographic Waves*

Depending on the pH of the solution, chloranilic acid may exist in three forms: the undissociated form I, $C_6H_2O_4Cl_2$, which is yellow in colour; the singly charged form II, $(C_6HO_4Cl_2)^-$, which is deep violet; and the doubly-charged form III, $(C_6O_4Cl_2)^=$, which is pale violet (Schwarzenbach and Suter 1941; Thamer and Voigt 1952). The dissociation constants have been variously reported to be $8{\cdot}4\times10^{-2}$ and $3{\cdot}8\times10^{-3}$ (Thamer and Voigt 1952), or $1{\cdot}4\times10^{-1}$ and $6{\cdot}6\times10^{-4}$ (Schwarzenbach and Suter 1941), corresponding to pK_a values of 1·08 and 2·42, or 0·85 and 3·18 respectively. Thus at pH 2·2 the solution

will contain predominantly a mixture of forms II and III, whereas at pH values of 5 and higher practically form III only will be present. Hence the single step at pH values of 4·9, 7·1, and 9·0 is almost certainly due to reduction of one and the same molecular species, namely, form III, and consequently the value of the Ilkovič constant was found to remain unaltered over this pH range. At pH 2·2, the two A.C. and D.C. waves are most probably due to the two forms II and III. The small prestep on the D.C. polarogram at pH 12·0, which reaches a constant height with increasing concentration, and the A.C. wave corresponding to it, are probably caused by adsorption at the electrode of the reduced form (compare e.g. the behaviour of methylene blue (Brdička 1942*a*, 1947)).

The non-linearity of the A.C. polarographic calibration curves is expected with organic compounds (Breyer 1953 ; Breyer, Bauer, and Hacobian 1954).

(*b*) *Base Current*

The discontinuity in the A.C. polarograms of chloranilic acid (see E_1, Fig. 3) is similar to that found by Gorodezkaya and Frumkin (1938) when studying the influence of multilayers of insoluble substances on the capacity-voltage curves obtained at a mercury pool electrode. It may correspond to an adsorption-desorption process involving part of the multilayer and/or a change in the structure of the adsorbed film, such as " crystallization " (see e.g. Brdička 1942*b*, 1947 ; Heyrovský, Sorm, and Forejt 1947 ; Wiesner 1947 ; Koryta 1953).

(*c*) *Solutions Containing* cyclo*Hexanol and Chloranilic Acid*

To explain the type of behaviour shown in Figure 5 the following facts must be considered :

(i) Two A.C. waves are observed ; there were no corresponding D.C. steps, hence the waves are of the tensammetric type.

(ii) The base current of the supporting electrolyte was lowered at potentials both more positive and more negative than the positive tensammetric wave, indicating adsorption in both these ranges of potential. This can be understood by remembering that *cyclo*hexanol is an uncharged species, and is adsorbed by virtue of van der Waals' forces, whereas chloranilic acid exists as a negatively charged ion, and will therefore be held at the electrode mainly by coulombic forces. It follows that with increasing positive polarization the adsorption of chloranilic acid will increase whilst that of *cyclo*hexanol will decrease. Hence the positive tensammetric wave is an outcome of an exchange process at the electrode between the two adsorbable species, chloranilic acid being adsorbed at potentials more positive than the wave and *cyclo*hexanol at more negative potentials. This interpretation is also borne out by the fact that the D.C. step of chloranilic acid shifts to more negative potentials and its slope indicates increasing irreversibility when *cyclo*hexanol is added to chloranilic acid solution. In other words, *cyclo*hexanol and not chloranilic acid is adsorbed in the potential region where the reduction of chloranilic acid occurs.

(iii) The shift of the positive tensammetric wave towards the electrocapillary zero point with increasing concentration of chloranilic acid follows naturally from the same reasoning ; the higher the concentration of chloranilic

acid, the less is the polarization required to bring about displacement of *cyclo*hexanol from the interface by molecules of chloranilic acid.

(iv) The height of the wave will depend on the polarizabilities of the species involved, on the number of molecules taking part in the process, as well as on the nature of the supporting electrolyte (Breyer and Hacobian 1952). These quantities are not known in the present case, so that the height of the wave cannot be predicted theoretically. A further complication is that apparently chloranilic acid can form different types of surface films at the electrode, depending on the concentration and on the potential at the interface (see Section IV (*b*)).

(v) The negative tensammetric wave of *cyclo*hexanol is much less affected than is the positive wave by the presence of chloranilic acid. It seems likely that the shift of the negative wave at higher concentrations of chloranilic acid is due to some interaction between the molecules of reduced chloranilic acid and *cyclo*hexanol.

(*d*) *Analytical Application*

Conventional polarography cannot detect concentrations of chloranilic acid lower than 10^{-5}M, but may be used for analytical estimation at higher concentrations. A.C. waves, on the other hand, are observable at concentrations as low as 10^{-7}M at pH 2·2 and at pH 4·9 and as low as 5×10^{-7}M at pH 7·1. For concentrations above 10^{-5}M at pH 2·2 and at pH 4·9, or above 10^{-4}M at pH 7·1, the height of the A.C. wave does not vary very much with concentration of chloranilic acid. Thus, estimation of chloranilic acid may be carried out for concentrations between 10^{-7} and 10^{-3}M, by using conventional polarography at the higher concentrations and A.C. polarography at lower concentrations.

V. Acknowledgments

The authors wish to thank Mr. W. Hannan of these laboratories for the preparation of a pure sample of chloranilic acid and Dr. S. Hacobian of this School for stimulating discussions.

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ALTERNATING CURRENT POLAROGRAPHY OF ORGANIC COMPOUNDS

IV. PERINAPHTHENONE

By B. BREYER* and H. H. BAUER*

[*Manuscript received April* 18, 1955]

Summary

The behaviour of *peri*naphthenone at the dropping mercury electrode has been investigated by the combined techniques of conventional (D.C.) and alternating current (A.C.) polarography. Two D.C. steps were observed, but an A.C. polarographic wave was found only at the potential of the more positive D.C. step. Two tensammetric waves were also seen, one of which appears to be the outcome of multilayer adsorption or of a change in state of the adsorbed film.

I. INTRODUCTION

In the present paper, salient features of the polarographic behaviour of *peri*naphthenone are reported. The D.C. polarography of this compound has been fully investigated by Beckmann (1954), who found that the more positive of the two steps obtained corresponds to a reversible one-electron transfer leading to the formation of a free radical. Only one A.C. polarographic wave, corresponding to the first D.C. step, was observed.

II. EXPERIMENTAL

The apparatus used, including polarographs, thermostat, capillary, and buffer composition, were the same as described in Part II of this series (Breyer and Bauer 1955*a*).

*peri*Naphthenone was prepared by Dr. H. Silberman, Department of Pharmacology, University of Sydney.

III. RESULTS

(*a*) *D.C. Polarography*

The calibration curve of the first D.C. step was linear. The Ilkovič constant was found to be $3 \cdot 2 \times 10^2$ μA l. mole^{-1} ; its value remained unaltered throughout the pH/range investigated.

The half-step potentials changed with concentration, becoming at first more positive, and then more negative, with increasing concentration. The slope of the log-plot also changed with concentration.

Prewaves were observed at pH values below 5·1, and at pH 10·7 ; they were distinctly observable only in saturated solutions (Fig. 1) except at pH 5·1,

* Physico-Chemical Laboratories, Faculty of Agriculture, University of Sydney.

where they were discernible at concentrations from 10^{-4}M upward. In neutral and alkaline solutions, the D.C. polarogram showed a dip in the residual current (Fig. 1 (*e*), (*f*)).

(*b*) *A.C. Polarography*

The summit potentials changed with concentration in the same way as did the half-step potentials. Where a prestep was observed on the D.C. polarogram, the A.C. wave showed a corresponding kink (Fig. 1 (*a*)-(*c*)).

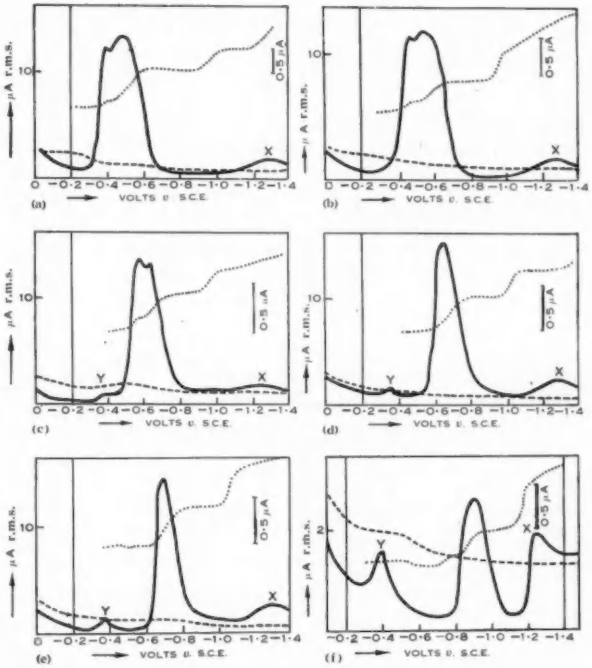

Fig. 1.—Polarograms of *peri*naphthenone at various pH values.

---- A.C. base current of buffer alone.

—— A.C. polarogram of buffer saturated with *peri*naphthenone.

···· D.C. polarogram of buffer saturated with *peri*naphthenone.

(*a*) pH 2·9 ; (*b*) pH 3·9 ; (*c*) pH 5·1 ; (*d*) pH 6·0 ; (*e*) pH 7·0 ; (*f*) pH 10·7.

At pH values up to 7·0, the A.C. wave *X* appeared at more negative potentials than the second D.C. step (Fig. 1 (*a*)-(*e*)) ; at pH 10·7, the wave corresponded rather closely in potential to the second D.C. step (Fig. 1 (*f*)). A further wave (*Y*, Fig. 1 (*c*)-(*f*)) was observed at more positive potentials than the first D.C. step.

The calibration curves of the A.C. wave which corresponds to the first D.C. step were non-linear (Figs. 2 and 3) and fitted the equation

$$i_{\sim(E_s)} = \frac{abC}{1+bC}, \qquad \ldots\ldots\ldots\ldots\ldots\ldots \quad (1)$$

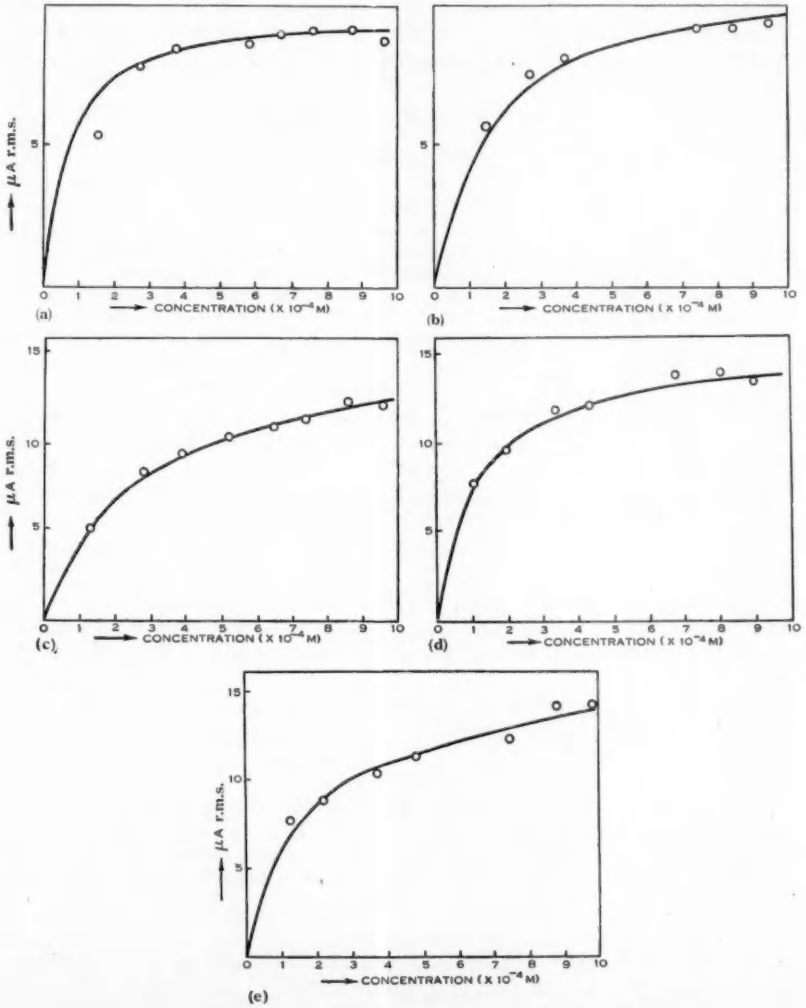

Fig. 2.—A.C. calibration curves of *peri*naphthenone (acid and neutral solutions).
○ Experimental points. —— Curve calculated from equation (1).
(*a*) pH 2·9; (*b*) pH 3·9; (*c*) pH 5·1; (*d*) pH 6·0; (*e*) pH 7·0.

where $i_{\sim(E_s)}$ is the alternating current at the summit potential, C the bulk concentration of *peri*naphthenone, and the adjustable parameters a and b have the values shown in Table 1.

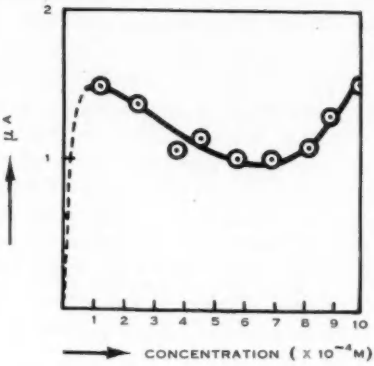

Fig. 3.—A.C. calibration curve of *peri*naphthenone at pH 10·7.

⊙ Experimental points.

---- Curve of best fit.

IV. Discussion

The lowering of the base current on both sides of the A.C. polarographic wave (Fig. 1) shows that both the oxidized and reduced forms produced during the first D.C. step are adsorbed at the electrode.

Table 1

PARAMETERS DESCRIBING THE A.C. CALIBRATION CURVES

pH	a (μA)	b (l. mole^{-1})
2·9	9·8	$1{\cdot}5 \times 10^4$
3·9	11·4	$5{\cdot}6_5 \times 10^3$
5·1	15·8	$3{\cdot}2 \times 10^3$
6·0	15·6	$6{\cdot}1_5 \times 10^3$
7·0	15·1	$5{\cdot}2_5 \times 10^3$

The wave X (Fig. 1 (*a*)-(*e*)) is of the tensammetric type since there is no corresponding D.C. step. The tensammetric wave seems due to desorption of the reaction product formed during the second D.C. step, since it occurs at potentials more negative than that step. At pH 10·7 (Fig. 1 (*f*)) the wave X corresponds rather closely in potential to the second D.C. step, and thus may be due either to desorption of a substance produced in the first or second stage of reduction, or alternatively may represent a combined reduction-tensammetric process.

The wave *Y* is also of tensammetric type, since there is no corresponding D.C. step; however, the base current lowering on both sides of the wave is not observed with normal tensammetric waves, where at potentials closer to the electrocapillary zero the electrode is covered by a film, while at greater polarizations the normal ionic double layer persists. The wave *Y* is similar to one observed with chloranilic acid (see Part III of this series, Breyer and Bauer 1955*b*). Once again two possibilities can be envisaged:

(i) The wave corresponds to a change in structure of the adsorbed film: for instance, the film may be a "mobile" one in one region of potential, changing into the "crystallized" state at other potentials (cf. Brdička 1942, 1947; Heyrovský, Sorm, and Forejt 1947; Wiesner 1947; Koryta 1953).

(ii) Several adsorbed layers may be present at the electrode (cf. Frumkin, Gorodezkaya, and Chugunov 1934; Gorodezkaya and Frumkin 1938; Voriskova 1947; Loveland and Elving 1952; Melik-Gaikazyan 1952), and the wave is due to an adsorption-desorption process involving part of the adsorbed material.

The dip in the residual current on the D.C. polarogram (Fig. 1 (*e*), (*f*)) is probably the outcome of the same phenomena.

V. Acknowledgment

Thanks are due to Dr. H. Silberman, Department of Pharmacology, University of Sydney, for the supply of a sample of pure *peri*naphthenone.

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THE VAPOUR PRESSURE OF SOLID CADMIUM

By T. A. O'Donnell*

[*Manuscript received March* 29, 1955]

Summary

An apparatus has been designed for measurement by the Knudsen effusion method of the vapour pressure of solid cadmium in the temperature range 200–260 °C. Reliability of the apparatus was checked by measurement of the vapour pressure of zinc, for which a recent, reliable determination has been reported.

The vapour pressure of cadmium in the temperature range studied is given by the equation

$$\log_{10} p_{\mathrm{mm}} = 9{\cdot}413 - \frac{6078}{T}.$$

I. Introduction

An examination of the literature has revealed considerable uncertainty in the values for the vapour pressure of solid cadmium. The only experimental determination was that of Egerton (1917) who used an effusion method. In his work, temperature measurement and control, collection of effusing vapour, and the vacuum attained were not sufficiently good for accurate results. He did not consider the effect of orifice thickness on effusion. In a subsequent publication not concerned with cadmium (Coleman and Egerton 1935) it was stated that the earlier work was not accurate.

Confusion regarding the volatility of cadmium arises from a typographical error in the vapour pressure equation in the paper of Maier (1926), who is frequently quoted as providing adjusted vapour pressures for solid and liquid cadmium and zinc.

Reference to the review by Ditchburn and Gilmour (1941) shows that the effusion method, due to Knudsen (1909*a*, 1909*b*), has been used frequently to measure vapour pressures of solids and liquids below 10^{-2} mm of mercury. The weight G of a vapour of molecular weight M in equilibrium with its condensed phase at absolute temperature T which passes through an orifice of area a into an evacuated space in 1 sec is related to the vapour pressure p according to the following equation :

$$G = p.a(M/2\pi RT)^{\frac{1}{2}}. \quad \ldots\ldots\ldots\ldots\ldots \quad (1)$$

In the work described here this method has been used to determine the vapour pressure of solid cadmium within the range 200–260 °C.

* Chemistry Department, University of Melbourne.

II. Design of Apparatus

A calculated fraction of the vapour issuing from the orifice of an effusion cell was condensed on a target and determined by direct weighing on a Kuhlmann microbalance. All weighings were made in terms of the rider only, and an absolute calibration of the rider was performed at Defence Standards Laboratories, Melbourne.

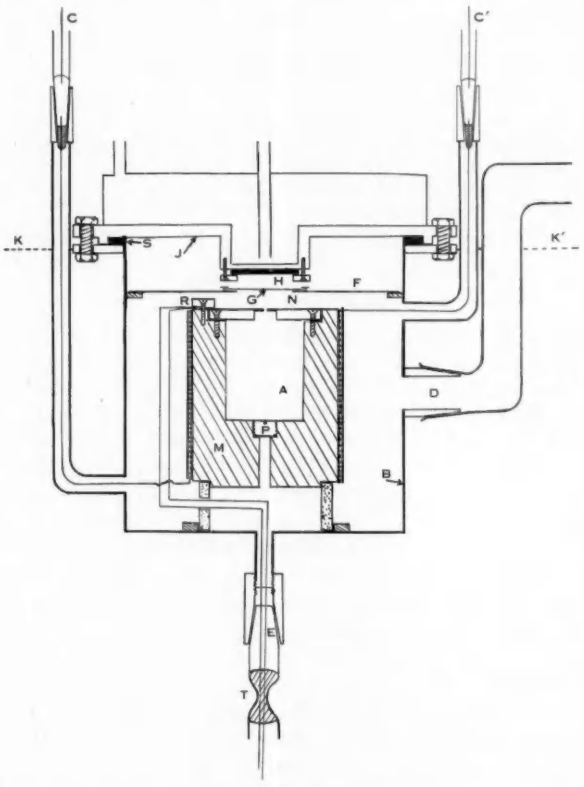

Fig. 1.—Effusion apparatus.

The apparatus used is shown in Figure 1. The effusion cell A is a cavity in a steel block M covered with a stainless steel top-plate N in the centre of which is the orifice. The block, supported on a refractory ring, is heated directly with "Nichrome" resistance tape, insulated from the block by glasscloth, which is also used to cover the windings. Due to the size of the block, the temperature could be controlled within the limits $\pm 0{\cdot}25$ °C by manual control of a Variac autotransformer.

The chromel-alumel thermocouple was introduced at *E* by means of a simple wax and glass seal *T*. The hot junction was hammered in the cold to give a flat leaf and then annealed. It was clamped to the block *M* at *R* under a steel plate. The cold junction was maintained at 0 °C and e.m.f.'s were measured with a Tinsley potentiometer (type 3184). The thermocouple was calibrated before and after the vapour pressure measurements at the freezing points of samples of tin, cadmium, and zinc of high purity.

Over most of its area, the top-plate *N* is $\frac{3}{16}$ in. thick. A thin edged orifice is provided in the central section, this section being 0·0035 in. thick and 0·25 in. in diameter. The area of the orifice was determined very accurately by optical enlargement and found to be 0·0184 cm², so that its diameter is 1·53 mm.

These orifice dimensions should be considered in terms of certain requirements of the Knudsen equation in its form above.

(i) The orifice should be infinitely thin. If it is not, some molecules, striking its walls, will suffer non-specular reflection and return to the effusion cell. Clausing (1932) calculated a factor *W* giving the probability that a molecule impinging on an orifice of finite thickness will pass through it. For the present apparatus, the factor $W=0\cdot943$ must be used in the vapour pressure equation.

(ii) The ratio of the orifice diameter to the mean free path of the vapour must be considerably less than unity to ensure collision-free molecular flow through the orifice. Schadel and Birchenall (1950) have shown experimentally that the ratio can be as great as 0·1, but they regard this as an upper limit. Since the mean free path is about 1·5 cm for a metal vapour at 600 °K and 10^{-2} mm pressure, this latter is the greatest pressure which can be measured using the orifice described here.

(iii) The area of the orifice must be considerably less than the effective evaporating area of the sample. This is to ensure that the rate of evaporation always exceeds the effusion rate and the equilibrium between vapour and condensed phase is not disturbed by the loss of molecules through the orifice. In the present work, the sample was a fairly massive piece of metal, together with some coarse filings.

The cylindrical brass vacuum chamber *B* is surrounded by a cooling tank (the level of the cooling water being as shown at *K*,*K'*) and is fitted with a removable bronze cover-plate *J*. In the centre of the cover-plate is a well carrying the target *H*, which is cooled by water circulating through a cooling head soldered to the plate as shown. This cooling causes the impinging vapour to condense on the target and on the underside of the lid.

The power leads are introduced through vacuum seals at *C* and *C'* and connection to the vacuum system is made at *D*. The pressure at operating temperature was always less than 10^{-5} mm Hg. At this pressure, scattering of the effusing beam is negligible. The vapour passing through a 1 in. central hole in the copper radiation shield *F* can be interrupted by a tinplate shutter, operated by an external magnet. This provided very accurate timing of runs.

The gasket *S* cut from $\frac{3}{16}$ in. "Hycar OR 15" rubber and lightly coated with "Apiezon grease N", is enclosed by two spacer rings $\frac{1}{8}$ in. deep which, on

compression, bear against the cover-plate and flange respectively. This arrangement provides a definite setting of the target relative to the orifice.

A calculable fraction of the weight G of vapour which issues from the orifice impinges on the target. The weight impinging G' is related to G as $G'=f.G$, where f can be shown from the cosine distribution law to be

$$f=\frac{r^2}{r^2+d^2},$$

where r is the radius of the target and d the distance between the orifice and the target. Speiser and Johnston (1949) have checked experimentally on the reliability of this relation.

The radius r can be measured accurately from the inner diameter (1·014 in.) of the collar which clamps the target H to the cover-plate J. The distance d, fixed definitely by the gasket design described above, can be measured under working conditions. The sealing plug P, shield F, and top-plate N are removed and the glass cone E is replaced by a plastic cone through which passes a close-fitting greased brass rod. With the furnace evacuated, the rod is brought against the target H and its length protruding from the plastic cone measured with a micrometer depth gauge. With N replaced, the length protruding is measured when the rod touches the area surrounding the orifice. The difference between the two micrometer readings gives the distance d which was reproducible to within 0·001 in. The determined value of f was 0·320.

III. Experimental Procedure and Conditions

In a recent determination, Vance and Whitman (1951) obtained vapour pressure values for solid zinc which appear reliable. As a check on the effective working of the apparatus, the vapour pressure of zinc was measured and compared with Whitman's value. The procedure used in this determination was the same as that followed subsequently with solid cadmium. The zinc and cadmium used were 99·95 per cent. pure, as supplied by the Electrolytic Zinc Co. of Australasia Ltd.

For each run, a fresh sample was introduced into the effusion cell. The top-plate N of the cell and the thermocouple were screwed firmly into place, and a check was made that the orifice was located centrally in the vacuum chamber. The radiation shield was introduced with the shutter closed.

A target suitably prepared and accurately weighed was affixed to the cover-plate J of the furnace and this plate was seated on the gasket, which was compressed initially by evacuation of the chamber. Then the bolts were tightened until the spacer rings were in contact with the opposite surfaces. After the system had been pumped to a pressure of about 10^{-6} mm the furnace block M was heated to a temperature about 10 °C above that required, allowed to cool and maintained for 15 min at the required temperature by setting the voltage to a previously determined value. This ensured temperature uniformity throughout the block and top-plate and equilibrium between solid and vapour. With the furnace pressure below 10^{-5} mm the shutter was opened. The temperature was checked regularly and the run was terminated by drawing back the shutter. The furnace was filled with hydrogen to stop effusion and to

accelerate cooling while providing protection from oxidation. After pumping out hydrogen, the cover-plate was removed, and the target demounted and weighed.

Considerable difficulty was encountered, particularly with cadmium, in obtaining complete condensation of all vapours impinging on the target. Minute traces of grease caused partial reflection of vapour. Wood (1916) and Langmuir (1917) had stated that cadmium vapour condenses quantitatively on metallic cadmium at room temperature. Accordingly a brass disk was coated with cadmium by evaporation and was used as the target. For the cadmium surface which had been exposed to the air, the accommodation coefficient was found to be less than unity. With brass targets, traces of sulphide and inorganic salt on the surface caused partial reflection of the vapour. The targets finally used were brass disks etched with nitric acid, boiled several times with distilled water, and washed in a modified Soxhlet apparatus with sulphur-free benzene.

TABLE 1

COMPARISON OF VAPOUR PRESSURE DATA

Condensate Wt., G' (g)	Temperature, T (°K)	Effusion Time, t (sec)	Vapour Pressure, p (mm)	
			Present Work	Vance and Whitman (1951)
$1{\cdot}09\times10^{-3}$	591·7	2710	$3{\cdot}73\times10^{-3}$	$3{\cdot}85\times10^{-3}$
$1{\cdot}08\times10^{-3}$	591·0	2710	$3{\cdot}69\times10^{-3}$	$3{\cdot}73\times10^{-3}$

With targets prepared in this way, observed vapour pressures for zinc agreed with expected values. Additional evidence regarding complete condensation on the target could be obtained from the pattern of condensation on the radiation shield. When some reflection of vapour occurred, that is, when imperfectly coated patches were observed on the targets, there was a definite shadow of the shutter on the upper surface of the radiation shield; but this shadow did not occur when condensation on target and cover-plate occurred. Providing targets were carefully prepared, water cooling was sufficient for collection of vapour. The apparatus was modified to allow dry ice-acetone cooling of the target, but this was found to be unnecessary. Blank runs were performed and condensation patterns were used to ensure that there was no reflection from the radiation shield or from the cover-plate, since such reflection would cause high vapour pressure values. These components were acid-washed before each run.

The Knudsen equation can be rewritten with the insertion of numerical values for the constants as

$$p_{\mathrm{mm}}=\frac{17{\cdot}14G'}{atWf}\left(\frac{T}{M}\right)^{\frac{1}{2}}, \quad \ldots\ldots\ldots\ldots\ldots \quad (2)$$

where the new terms are G', the weight of condensate (g) collected on the target in t sec, f the fraction of total effusion vapour which impinges on the target, and W the Clausing probability factor. With $a=0{\cdot}0184$ cm^2, $W=0{\cdot}943$, and $f=0{\cdot}320$, vapour pressures for zinc were determined from the data in Table 1 and compared with values calculated from Vance and Whitman's equation.

The agreement between the values obtained in the present work and by Vance and Whitman indicated that the apparatus gave reliable results.

IV. The Vapour Pressure of Cadmium

The vapour pressure of solid cadmium was determined in the temperature range 200–260 °C using the apparatus and procedure exactly as described for zinc, which was used merely to check the reliability of the apparatus. Calculations were based on the equation quoted above, the values of a and W being as before. However, f has the value 0·320 for the first four runs and 0·326 thereafter. Brewer (1950) has shown from Gaydon's spectroscopic data that the species Cd_2 is negligible in cadmium vapour. Hence M is taken as 112·4. Measured values of T, t, and G' and calculated values of p are given in Table 2.

Table 2

Experimental values of T, t, and G' also calculated values of p

Temperature, T (°K)	Effusion Time, t (sec)	Condensate Wt., G' (g)	Calculated Vapour Pressure, p (mm)
533·5	1200	$1·85\times10^{-3}$	$1·03\times10^{-2}$
521·3	1808	$1·63\times10^{-3}$	$5·94\times10^{-3}$
513·8	3600	$2·18\times10^{-3}$	$3·96\times10^{-3}$
505·3	3600	$1·28\times10^{-3}$	$2·31\times10^{-3}$
498·0	5400	$1·35\times10^{-3}$	$1·58\times10^{-3}$
488·7	7500	$1·13\times10^{-3}$	$9·45\times10^{-4}$
481·5	10800	$1·09\times10^{-3}$	$6·28\times10^{-4}$

V. Vapour Pressure Equation and Latent Heat of Sublimation

These experimental results with those of Egerton are shown graphically in Figure 2. A least squares analysis of the present values gives the following vapour pressure equation

$$\log_{10} p_{\mathrm{mm}} = 9·413 - \frac{6078}{T}. \quad \ldots\ldots\ldots\ldots \quad (3)$$

From this equation ΔH_{500} has the value $27·8 \pm 0·4$ kcal mole^{-1}.

The variation of the latent heat of sublimation with temperature was determined from the difference in molar heat capacities of the two phases (Kelley 1949) to be

$$\Delta H_T = \Delta H_0 - 0·34T - 1·47\times10^{-3}T^2, \quad \ldots\ldots\ldots \quad (4)$$

H_0 was found to be 28·4 kcal from a least squares analysis of a Σ plot as recommended by Kelley (1935).

The value of ΔH_0 usually quoted for solid cadmium is that of 27·01 kcal calculated by Kelley (1935) from specific heats, the latent heat of fusion and a latent heat of evaporation, derived from a vapour pressure equation for the liquid.

However, Lumsden (1952) comments that the vapour pressure values for liquid cadmium in the vicinity of the melting point are not as inter-consistent

as at higher temperatures, and that different workers report variations in the heat of fusion from 1155 to 1540 cal mole^{-1} and in the specific heat of the liquid from 6·62 to 7·41 cal deg^{-1} mole^{-1}.

Maier (1926) used the vapour pressure values of Braune and of Fogler and Rodebush and Braune's specific heat value and calculated ΔH_0 for the liquid as 26·68 kcal. Using latest figures for the heat of fusion, this would give a value of 27·7 kcal for ΔH_0 for the solid.

Egerton (1917) also gave this value of 27·7 kcal, although the slope of his curve for log p plotted against $1/T$ is not certain.

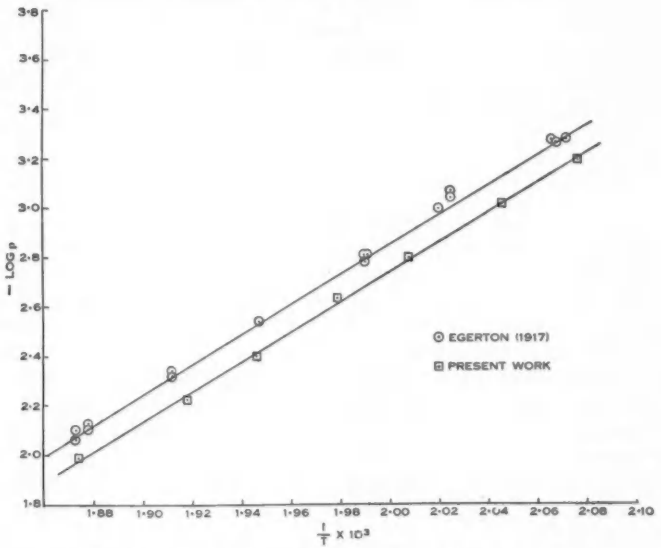

Fig. 2.—Plot of experimental results and Egerton's results.

VI. Acknowledgments

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MEASUREMENT OF THE VAPOUR PRESSURE OF BISMUTH BY A RADIOACTIVE TRACER TECHNIQUE

By T. A. O'Donnell*

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Summary

A radioactive tracer technique has been used to increase the sensitivity of the Knudsen method of vapour pressure determination. The vapour pressure of liquid bismuth in the temperature range 400 to 500 °C has been measured and is given by the equation

$$\log_{10} p_{\mathrm{mm}} = 9 \cdot 390 - \frac{10500}{T}.$$

I. Introduction

The range of vapour pressures over which measurements can be made using the Knudsen effusion method is limited. As given in a previous paper (O'Donnell 1955) the mean free path of the vapour must be much greater than the diameter of the effusion orifice. At pressures somewhat greater than 10^{-2} mm Hg, the mean free path approaches in magnitude the dimensions of the smallest orifice which can be used conveniently. The weight of vapour effusing in unit time is so small at pressures below 10^{-4} mm that if a direct weighing technique is to be used, the time for an effusion run becomes inconveniently large. Erway and Simpson (1950), Phipps *et al.* (1950), Phipps, Sears, and Simpson (1950), Hall (1951), and Schadel and Birchenall (1950) applied radioactive tracers to the effusion technique to increase the sensitivity of the method.

In the work described here, the vapour pressure of liquid bismuth was determined using the same apparatus and procedure previously described (O'Donnell 1955) with an isotopic mixture of bismuth in the effusion cell. An "unweighable" quantity of effusing vapour, condensed on the target, was determined by its activity which was compared with that of the weighed isotopic mixture. From this, the weight of condensate and the vapour pressure at the particular temperature were calculated.

II. Preparation of Radioactive Bismuth Source

An isotope ^{210}Bi, having radiation characteristics suitable for this work, occurs as the daughter product RaE of the lead isotope RaD. As the first step in the preparation of radioactive metallic bismuth, lead dioxide containing RaD and daughter products was dissolved in nitric acid in the presence of hydrogen peroxide. Bismuth nitrate was added as carrier and the solution

* Chemistry Department, University of Melbourne.

was made strongly alkaline with sodium hydroxide ; the bismuth remained as insoluble hydroxide while the solution contained sodium plumbite. The precipitate was dissolved and reprecipitated four times, with the addition each time of lead nitrate as hold-back carrier.

The bismuth hydroxide was dissolved in the minimum amount of nitric acid to prevent hydrolysis and an iron rod was rotated in the solution. Spongy metallic bismuth was deposited by electrochemical displacement on the iron. It was then removed with a jet of acetone and transferred to the silica boat *B* in the apparatus shown in Figure 1, in which metallic bismuth was vapourized on to a steel disk. The essential feature of this apparatus is a small effusion cell *E*, with sealing plug *P*, and an orifice *O* of similar dimensions to the orifice used subsequently in the vapour pressure measurements. The cell was heated

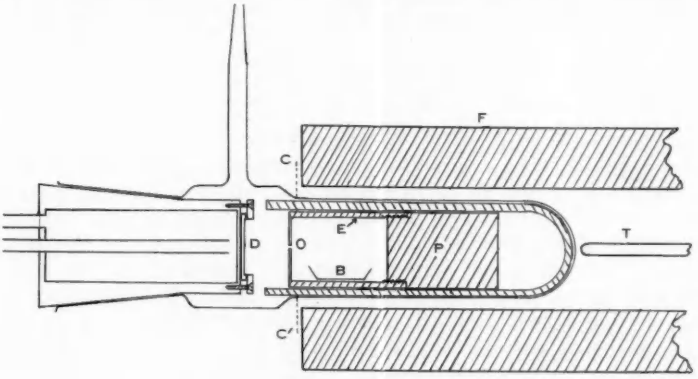

Fig. 1.—Effusion apparatus.

by transfer along a steel liner from an external muffle furnace *F*. The heated section of the glass envelope was of Supremax glass joined at *C*,*C'* to a Pyrex B45 socket. Into this was fitted a hollow water-cooled brass B45 cone, to the inner face of which was held by a collar, the 1 in. dished stainless steel disk *D*. The distance between disk *D* and orifice *O* was made equal to that between the corresponding components of the vapour pressure apparatus, so that the distribution of condensed bismuth on the targets in each case was the same. The B10 sidearm connected with a pumping system capable of providing a pressure of 10^{-6} mm in the vapourization apparatus. In this apparatus weights of about 2 mg (weighed to 10 μg) of an isotopic mixture were prepared as sources for the vapour pressure runs.

Both the electrodeposition and vapourization provided separation of lead from bismuth additional to that obtained in the chemical separation process, because the deposition potentials for lead and bismuth are about 0·3 V apart and because a dilute solution of lead in bismuth would exert a very small partial pressure of lead.

The radiochemical purity of the ^{210}Bi prepared in this way was checked by following the decay of activity for 50 days. Since ^{210}Bi has a half-life of 4·989 days, the 1·17 MeV β-activity from the original bismuth will have decayed to a negligible level in this time. ^{210}Pb emits β-radiation with an energy of 0·025 MeV which would not be detected by an end-window Geiger-Müller counter. However, its half-life is 22 years and so it will come into equilibrium with RaE and any residual RaE activity after a prolonged period will be an indication of the RaD in the original RaE sample. After 50 days, the activity of the source disk had dropped to 0·1 per cent. of its initial value and curvature of the plot of logarithm of activity *against* time was slight. Hence the RaD contamination was well below 0·1 per cent.

III. Experimental Procedures

(*a*) *Effusion Apparatus*

The apparatus described in the preceding paper (O'Donnell 1955) was employed. Tammann and Ruhenbeck (1935) report that there is no reaction between liquid bismuth and iron below 1000 °C and microscopic examination of the preparations used here shows that the droplets formed when the bismuth source is heated *in vacuo* do not wet the steel disk. The subdivision of the sample into small droplets ensures that the evaporating surface is large by comparison with the area of the orifice and that the cell is saturated with vapour.

The target-disks, held to the underside of the cooling well, were similar to the source disk. They were carefully cleaned by hot washing in acid, distilled water, and benzene, although it was demonstrated directly that bismuth vapour condensed easily on metal surfaces at room temperature.

The procedure during a vapour pressure measurement was as given in the previous paper. After the shutter had been drawn back to terminate a run, hydrogen was admitted to the furnace to accelerate cooling and to prevent oxidation of the source.

(*b*) *Counting of Samples*

The activities of the source disks and targets were determined using conventional counting equipment with an end-window Geiger-Müller counter. The sample could be located in the castle on one of three shelves, so that disks of widely varying activity could be counted, the shelf factors being determined with disks of convenient activity.

Since source and target disks were similar, no backscattering correction was necessary in the comparison of activities. Also source and target disks were coated by effusion from similar orifices and so the distribution of metal over all disks, governed by the cosine distribution law, was similar. Therefore, it was not necessary in counting to apply geometry corrections for sample distribution. Since the β-radiation from ^{210}Bi is of high energy, self-absorption corrections were not necessary for the very thin samples counted. This effect was found to be negligible for bismuth thicknesses up to 2 mg per cm^2. U_3O_8 was used as a β-emitting standard to detect any changes in the sensitivity of the

counting equipment. Decay corrections were based on the value for the half-life of bismuth given by Lockett and Thomas (1953) as $4 \cdot 989 \pm 0 \cdot 013$ days. Coincidence corrections were applied in the case of the more active source disks.

IV. Measurement of Vapour Pressures

Since the weight of condensate on a target is calculated from the ratio of its activity to that of the weighed source material, there is the possibility of a systematic error in a series of determinations using a single source disk. Accordingly, two series were performed and the results for 10 runs in which experimental conditions were satisfactory are listed in Table 1.

Table 1

Data from 2 series of runs

Source Disk	Target	Activity* (count/min)	Calculated Condensation Wt., G'' (g)	Temp., T (°K)	Effusion Time, t (sec)	Vapour Pressure, p (mm)
Series A	A–1†	97	$3 \cdot 62 \times 10^{-5}$	770·8	3600	$4 \cdot 10 \times 10^{-5}$
Wt. of bismuth	A–2	98	$3 \cdot 68 \times 10^{-5}$	761·5	3600	$4 \cdot 14 \times 10^{-5}$
$1 \cdot 81 \times 10^{-3}$ (g)	A–3	96	$3 \cdot 61 \times 10^{-5}$	752·0	5400	$2 \cdot 69 \times 10^{-5}$
Activity 4840	A–4	84	$3 \cdot 14 \times 10^{-5}$	742·5	7200	$1 \cdot 75 \times 10^{-5}$
(count/min)	A–5	38	$1 \cdot 43 \times 10^{-5}$	726·3	7200	$7 \cdot 86 \times 10^{-6}$
	A–6	16·8	$6 \cdot 30 \times 10^{-6}$	700·5	9900	$2 \cdot 47 \times 10^{-6}$
Series B	B–4	15·9	$8 \cdot 13 \times 10^{-6}$	709·0	8100	$3 \cdot 92 \times 10^{-6}$
Wt. of bismuth	B–5	40·7	$2 \cdot 08 \times 10^{-5}$	732·5	7800	$1 \cdot 06 \times 10^{-5}$
$1 \cdot 61 \times 10^{-3}$ (g)	B–6	24·5	$1 \cdot 25 \times 10^{-5}$	723·2	7200	$6 \cdot 87 \times 10^{-6}$
Activity 3150	B–7	9·5	$4 \cdot 86 \times 10^{-6}$	682·3	18000	$1 \cdot 03 \times 10^{-6}$
(count/min)						

* Corrected.

† Target from run No. 1 of series A.

Vapour pressures were calculated from the equation

$$p_{\mathrm{mm}} = \frac{17 \cdot 14 G''}{f a W t} (T/M)^{\frac{1}{2}}, \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (1)$$

where f, a, and W have the values 0·320, 0·0184, and 0·943 cm² respectively (see O'Donnell 1955) and where t, T, and M are the effusion time, the absolute temperature at which the pressure is measured, and molecular weight of the vapour; and G'' is the calculated weight of condensate.

Some activities recorded in Table 1 are little greater than the background count of about eight counts per minute, implying a lack of accuracy in the measurements. The values listed above were calculated for comparison with the activity of the source disk counted in the lowest shelf, and were obtained after application of shelf factors and other corrections to actual counts for target disks in different positions in the castle. In all determinations, sufficient counts were recorded to ensure that the counting error was less than 2 per cent.

V. Atomicity of Bismuth Vapour

In calculating vapour pressure from the equation above, bismuth has been assumed diatomic in the vapour state in the temperature range studied.

Zartmann (1931) and Ko (1934) studying the distribution of molecular velocities in a molecular beam of bismuth showed that at about 850 °C the vapour contains about 40 per cent. Bi and 60 per cent. Bi_2, although Ko claimed to have demonstrated the presence of the species Bi_8 to the extent of about 2 per cent.

A direct determination of the vapour pressure of liquid bismuth and the atomicity of the vapour was undertaken by Yoshiyama (1941), who quotes an equation for the variation of molecular weight of the vapour with change in absolute temperature,

$$\log M = \frac{532 \cdot 722}{T} + 1 \cdot 931. \quad \ldots\ldots\ldots\ldots\ldots (2)$$

This equation is based on his vapour pressure values and on certain experimental factors peculiar to his own apparatus. Yoshiyama's apparatus will be criticized below and his vapour pressures are in doubt. Hence the equation can be regarded as giving only the order of the molecular weight at any temperature. At the extremes of the temperature range studied in the present work, namely 400 and 500 °C, the equation gives values of 530 and 420 for the molecular weight.

Honig (1953, 1954*a*, 1954*b*), in mass spectral analysis of the Group IV elements, has found moderate concentrations of polyatomic ionic clusters in the vapour phase. He has shown that for carbon polyatomic molecules containing up to eight atoms participate in the sublimation process. Clusters of seven atoms were found for germanium and silicon, five for tin, and two for lead.

In the light of this work, it may be difficult to ascribe a definite atomicity to the vapour of an element. Therefore, in the absence of reliable evidence as to the atomicity of bismuth vapour, M has been taken as 418 in the vapour pressure equation in the present work.

VI. Discussion of Reported Vapour Pressures for Bismuth

Even at relatively high vapour pressures there is poor agreement between published values for liquid bismuth. There are no reliable values reported for pressures below 10^{-3} mm Hg. Previously reported values are shown in Figure 2, with those from the present work.

Weber and Kirsch (1940) used a method based on that of Rudberg (1934) which was supposed to be an effusion technique. Their pressures calculated for one temperature differ by 30 per cent., although they claim an accuracy better than 1 per cent. in determining the amount of effusing vapour. Whitman (1952) has shown that in such an apparatus liquid-vapour equilibrium would not be established. Results could be as low as 20 per cent. of actual values although one factor not easily calculated tends to increase the values by an unknown amount.

Weber and Plantenberg (1946) did not claim accuracy in their single point determination. Yoshiyama's (1941) results obtained using the technique of Volmer (1931) show the greatest self-consistency as tested by a Clausius-Clapeyron plot. He points out the agreement between his vapour pressure figures and those of Weber and Kirsch, which it is now known would be expected to be very low. Extrapolation of Yoshiyama's values indicates that they are about 40 per cent. of those obtained in the present work.

There are several possible sources of error in Yoshiyama's work. The thermocouple was placed near but not in contact with the effusion cell and each was irradiated by a furnace outside the vacuum system. His indirect

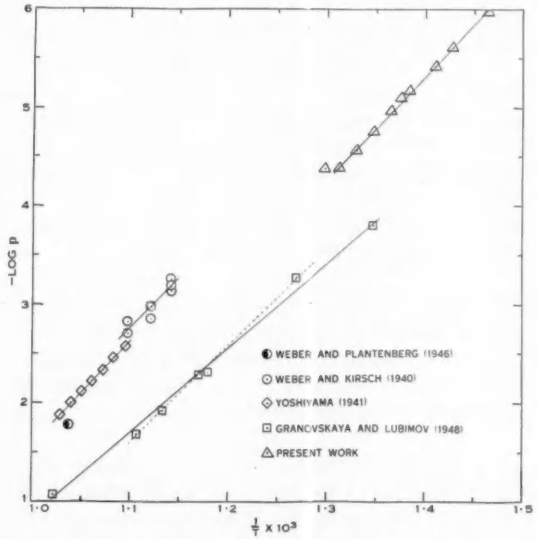

Fig. 2.—Present and previously reported vapour pressure values for liquid bismuth.

calculation of the Clausing probability factor W is obviously too high, as the value quoted implies that the silica in the region of the orifice has been ground to a thickness of 0·04 mm. No attempt was made to remove the oxide film which is known to retard surface evaporation from liquid bismuth. This is probably the main factor leading to low results, whereas Weber and Kirsch probably removed the oxide layer since they evaporated half the bismuth sample before measuring the effusion rate. In this latter case, low values resulted from unsaturation of the cell.

The measurements of Granovskaya and Lubimov (1948) do not appear reliable. The points on the graph of log p *against* the inverse of the absolute temperature are not collinear. These workers used the Langmuir rate of evaporation method, in which the area of the surface of the liquid must be

known accurately. No details of measurement of surface area are given, nor is a value quoted. There has apparently been no consideration given to wetting by the liquid metal of the crucible or of the silica thermocouple sheath.

In the present work the results for the first three runs of series *B* have been omitted from Table 1, since the targets became contaminated by radioactivity and results were meaningless. All other results are included in Table 1 and represented on Figure 2. A low result was obtained in run *A*–1. Since, after a run, the apparatus was always cooled from 400–500 °C in hydrogen, *A*–1 is the only run in which the source material had not been heated in hydrogen prior to the run. So, although this single determination is not conclusive, it indicates that vapourization may have been retarded by an oxide layer.

All targets, with the exception of that from run *A*–5, were evenly coated, any difference in appearance being due to a gradual diminishing of the thickness of the deposit from the centre to the outer edge. In run *A*–5, the deposit occurred as a wide spot at the centre of the target, the outer edge being very thinly coated. Collimation of the issuing vapour stream and the low result obtained could occur, if some abnormal cooling conditions caused condensation at the edge of the orifice. The remaining runs, *A*–2 to *A*–4, *A*–6, and *B*–4 to *B*–7 are, then, the only runs in which experimental conditions are acceptable.

VII. Vapour Pressure Equation and Latent Heat of Vapourization

Because of the uncertainty as to whether bismuth vapour is exclusively diatomic in the temperature range studied, the simple form of the vapour pressure equation, derived from a least squares analysis of the values obtained, is given as

$$\log_{10} p_{\mathrm{mm}} = 9 \cdot 390 - \frac{10500}{T}. \quad \ldots\ldots\ldots\ldots \quad (3)$$

From this equation can be calculated a formal latent heat of vapourization for the mean temperature of this range, 720 °K,

$$\Delta H_e = 48 \cdot 1 \pm 0 \cdot 6 \text{ kcal mole}^{-1}.$$

This is very close to the value of 47·3 kcal mole^{-1} calculated by Yoshiyama for the mean temperature 943 °K. Granovskaya and Lubimov gave a value of 38·61 based on the line of best fit for their points (solid line in Fig. 2). It is interesting to note that, if the two end-determinations be neglected, the remaining points fit quite well to a line (shown as dotted in Fig. 2) and that its slope gives a latent heat of about 45 kcal mole^{-1}.

VIII. Acknowledgment

The author wishes to thank Associate-Professor A. N. Hambly for many helpful discussions.

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LIQUID–VAPOUR EQUILIBRIA

VII. THE SYSTEMS NITROMETHANE+BENZENE AND NITROMETHANE+CARBON TETRACHLORIDE AT 45 °C

By I. Brown* and F. Smith*

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Summary

The liquid-vapour equilibrium data are given for the systems nitromethane+benzene and nitromethane+carbon tetrachloride at 45·00 °C. These data are used to calculate the excess free energy of mixing for these systems.

I. Introduction

The liquid-vapour equilibria for the system nitromethane+benzene have been determined at atmospheric pressure by Weck and Hunt (1954). The present measurements were made to provide isothermal values of the excess free energy of mixing required for an investigation of the thermodynamic properties of solutions of polar liquids.

II. Experimental

(*a*) *Apparatus*

The liquid-vapour equilibrium and vapour pressure measurements were made by Brown and Smith's (1954*a*) methods. The nitromethane+benzene system was analysed by refractive index measurements using a Hilger-Chance precision refractometer maintained at 25·00±0·01 °C. The nitromethane+carbon tetrachloride system was analysed by density measurements as used by Brown and Ewald (1950).

Table 1

PHYSICAL PROPERTIES OF COMPONENTS

Property	Nitro-methane	Benzene	Carbon Tetrachloride
Boiling point/760 mm Hg (°C)	101·07	80·05	76·65
$d_4^{25\cdot00}$	1·13105	0·087366	1·58439
$n_D^{25\cdot00}$	1·37965	1·49792	1·45739
Vapour pressure 45·00 °C ..	93·72	223·74	258·84

(*b*) *Purification and Properties of Components*

The nitromethane was purified by the method used by Brown and Smith (1955), the benzene by the method described by Brown and Ewald (1951) and the carbon tetrachloride by the Barker, Brown, and Smith's (1953) method. The physical properties of the components are shown in Table 1.

* Division of Industrial Chemistry, C.S.I.R.O., Melbourne.

(c) *Analytical Methods*

Liquid and vapour samples from the system nitromethane+benzene were analysed by refractive index measurements. The refractive index-composition data obtained from mixtures prepared by weighing are given in Table 2, where x_1 is the mole fraction of nitromethane in the mixture. The method of Brown and Smith (1954*a*) was employed to calculate the composition of samples.

TABLE 2

NITROMETHANE+BENZENE

Refractive index; composition data

x_1	$n_D^{25\cdot00}$	x_1	$n_D^{25\cdot00}$
0·0448	1·49430	0·5075	1·44934
0·1077	1·48906	0·6006	1·43828
0·2037	1·48050	0·6993	1·42563
0·2897	1·47238	0·8033	1·41108
0·4083	1·46025	0·8992	1·39647
0·4878	1·45158	0·9506	1·38812

Liquid and vapour samples from the system nitromethane+carbon tetrachloride were analysed by density measurements. The density-composition data obtained on mixtures prepared by weighing are given in Table 3, where x_1 is the mole fraction of nitromethane in the mixture. The method of Brown and Smith (1954*b*) was employed to calculate the composition of samples.

TABLE 3

NITROMETHANE+CARBON TETRACHLORIDE

Density: composition data

x_1	$d_4^{25\cdot00}$	x_1	$d_4^{25\cdot00}$
0·0509	1·57004	0·5004	1·41904
0·1000	1·55612	0·5946	1·37782
0·2001	1·52628	0·7049	1·32326
0·2929	1·49638	0·8063	1·26601
0·3963	1·45997	0·8954	1·20870
0·4948	1·42138	0·9445	1·17373

III. Liquid-Vapour Equilibrium Data

The liquid-vapour equilibrium data are shown in Tables 4 and 5, where x_1 and y_1 are the mole fractions of nitromethane in the liquid and vapour respectively, P is the total pressure in standard mm Hg, and α is the relative volatility given by $\alpha = y_1x_2/y_2x_1$.

From graphs of the data in Table 4 it can be seen that at 45·00 °C this system forms an azeotrope with a mole fraction of 0·120 nitromethane at a total pressure of 228·0 mm Hg.

From graphs of the data in Table 5 it can be seen that this system forms an azeotrope with a mole fraction of 0·227 nitromethane at a total pressure of 303·0 mm Hg.

TABLE 4

NITROMETHANE + BENZENE AT 45·00 °C

Experimental data and derived functions

x_1	y_1	P	α	μ_1^E	μ_2^E	G_x^E
0·0445	0·0548	226·43	1·245	698·5	0·7	31·4
0·0966	0·1026	227·83	1·069	598·4	7·2	64·3
0·1979	0·1694	226·92	0·8266	457·8	31·3	115·7
0·2927	0·2173	223·50	0·6709	357·2	64·1	149·9
0·3921	0·2602	218·27	0·5453	270·7	109·7	172·8
0·4737	0·2942	213·14	0·4631	213·4	156·6	183·5
0·5259	0·3166	208·62	0·4176	180·0	189·2	184·4
0·6180	0·3543	200·11	0·3392	122·7	264·0	176·7
0·7118	0·4023	188·14	0·2725	74·8	355·1	155·6
0·8102	0·4765	170·13	0·2132	36·8	473·1	119·6
0·9051	0·6144	142·18	0·1671	15·1	606·8	71·3
0·9601	0·7708	117·19	0·1398	0·5	705·6	28·6

IV. DERIVED THERMODYNAMIC FUNCTIONS

The excess chemical potentials μ_1^E and μ_2^E and the excess free energy of mixing G_x^E were calculated from the equilibrium data using equations (**2**), (**3**), and (**4**) of Brown and Smith (1954*a*). The values obtained (cal/g-mol) are shown in Tables 4 and 5.

TABLE 5

NITROMETHANE + CARBON TETRACHLORIDE AT 45·00 °C

Experimental data and derived functions

x_1	y_1	P	α	μ_1^E	μ_2^E	G_x^E
0·0459	0·1296	287·42	3·095	1360	7·3	69·4
0·0918	0·1780	297·19	2·142	1141	23·3	125·9
0·1954	0·2217	302·91	1·173	812·4	77·5	221·1
0·2829	0·2368	302·56	0·7865	618·1	137·3	273·3
0·3656	0·2458	301·42	0·5655	477·9	205·0	304·8
0·4659	0·2532	298·86	0·3887	337·9	302·3	318·9
0·5366	0·2598	296·88	0·3031	260·5	382·5	317·0
0·6065	0·2657	293·27	0·2348	189·6	473·2	301·2
0·6835	0·2773	287·10	0·1777	127·7	587·7	273·3
0·8043	0·3138	264·65	0·1113	52·1	808·5	200·1
0·9039	0·4078	214·63	0·0732	13·3	1036	111·5
0·9488	0·5283	170·95	0·0604	4·5	1149	62·6

The values of the liquid molar volumes V_1 and V_2 and the second virial coefficient in the equation of state for the mixed vapours β_{12} were obtained by the methods given by Brown and Smith (1954*a*).

The value of the second virial coefficient for nitromethane was obtained from an equation given by Douslin (1954) which was based on the experimental data of McCullough *et al.* (1954). The value for benzene was obtained from the equation given by Allen, Everett, and Penney (1952) and that for carbon tetrachloride from the Berthelot equation.

The values of the second virial coefficients and molar volumes (l/mol) used for the system nitromethane+benzene at 45 °C were :

β_{11}	β_{22}	β_{12}	δ_{12}	V_1	V_2
−3·11	−1·23	−1·13	2·09	0·06	0·09

For the system nitromethane+carbon tetrachloride at 45 °C the values used were :

β_{11}	β_{22}	β_{12}	δ_{12}	V_1	V_2
−3·11	−1·24	−1·15	2·05	0·06	0·10

V. Discussion

For the system nitromethane+benzene at 45·00 °C the excess free-energy data were fitted by the method of least squares to equation (**1**) :

$$G_x^E = x_1 x_2 [a + b(x_1 - x_2) + c(x_1 - x_2)^2]. \quad \ldots\ldots\ldots\ldots \quad (1)$$

The values (cal/g-mol) of the constants and the standard deviation of the fit σ were

a	b	c	σ
741·8	42·7	0	2·0

These values do not indicate separation into two liquid phases. The thermodynamic consistency of the results was tested by the method used previously, the ratio of the areas above and below datum on a plot of $\mu_1^E - \mu_2^E$ *against* x_1 was 1·04. The error in G_x^E due to errors in the directly measured quantities was estimated to be 2·5 cal/mole.

For the system nitromethane+carbon tetrachloride at 45·00 °C the constants obtained in fitting the excess free-energy data to equation (**1**) were

a	b	c	σ
1275·6	−111·8	175·4	1·6

The ratio of the areas in the test for thermodynamic consistency was 1·001 and the errors in G_x^E due to those in the measured quantities were estimated to be 3 cal/mole.

VI. Acknowledgment

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GEOMETRIC ISOMERISM IN SOME UNSATURATED ALIPHATIC KETONES

By H. H. Hatt* and J. A. Lamberton*

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Summary

If ketones are prepared by heating unsaturated fatty acids at a high temperature in the presence of a metal or metallic oxide catalyst, some stereoisomeric change and movement of the double bond accompany ketonization. The ketones, oleone and erucone of the *cis-cis*-class, described in the literature as products of reactions of this kind, are shown to have been mixtures of isomers with *trans-trans*-forms predominating. Oleone and erucone, containing no detectable amounts of *trans*-material can be prepared either from the corresponding acyl chloride and triethylamine, or by condensation of the methyl or ethyl ester of the appropriate acid in xylene using sodium ethoxide as catalyst. These ketones are readily converted to the tetrahydroxy ketones and thence by oxidation to ketodibasic acids, useful as intermediates for the preparation of cyclic ketones.

I. Introduction

Saturated higher aliphatic ketones are obtained in good yield by heating the free fatty acid at elevated temperatures with a suitable metal or metallic oxide. Where this method has been used to prepare unsaturated aliphatic ketones, the yields reported have been disappointingly low and the melting points of ketones derived from the *cis*-acids unexpectedly high. Thus Easterfield and Taylor (1911) heated barium oleate or a mixture of the acid with iron filings at temperatures above 300 °C and obtained, in small yield, a crystalline compound of m.p. 59 °C which they regarded as oleone, the *cis-cis*-ketone. The greater portion of their product was a viscous oil which agreed in composition with oleone ; this they considered might be a mixture of ketones formed with some accompanying movement of double bonds. Breuer and Weinmann (1935) also found a crystalline compound of m.p. 58·5 °C among the products from the dry distillation of calcium oleate which they too regarded as oleone. Tressler (1934) in a patent claimed that the method of Easterfield and Taylor was improved if ketonization of oleic acid proceeded in an inert atmosphere, but did not describe the oleone obtained.

Easterfield and Taylor ketonized other unsaturated acids and met with similar experiences. From erucic acid (13-(*cis*)-docosenoic acid) a small yield of " erucone " was obtained which melted vaguely from 50 to 60 °C. The *trans*-acids, elaidic and brassidic acids, gave slightly better, but still small yields of the corresponding ketones ; elaidone, m.p. 70 °C and brassidone, m.p. 80 °C.

* Division of Industrial Chemistry, C.S.I.R.O., Melbourne.

Apart from the fact that at the high temperatures used in the preparations, *cis-trans*-conversion was likely, the identity of these *cis-cis*-unsaturated ketones seemed open to doubt because of their high melting points relative to those of the parent acids. We have repeated Easterfield and Taylor's ketonization of oleic acid and have obtained a small yield of a crystalline material, which after many crystallizations still melted over the range 59 to 63 °C. The analysis of this material fitted the requirements for a diheptadecenyl ketone and the substance hydrogenated readily to stearone. But it was not oleone for its infra-red spectrum showed the strong absorption band at 964 cm^{-1} typical of the out-of-plane CH deformation at a disubstituted *trans*-double bond. The intensity of the band was equivalent to the presence of 70 per cent. of elaidone or other isomeric *trans-trans*-ketone.

Recently, Clement (1953*b*) obtained unsaturated ketones in good yield by condensing the ethyl ester of the appropriate acid in xylene solution in presence of sodium hydride and hydrolysing the resulting β-keto ester with alkali. In this way, he obtained oleone, m.p. 40 °C and erucone, m.p. 48 °C.

We have prepared these two ketones from the corresponding acyl chlorides by way of the ketene dimer, following the method developed by Sauer (1947, 1951) for the preparation of saturated ketones. The oleone so prepared melted at 29 °C and the erucone at 51 °C. The typical absorption bands of the *trans*-compounds at 964 cm^{-1} could not be detected in the spectra of these ketones and considering the experimental accuracy, this means that less than 0·7 per cent. of the *trans*-isomers were present. Unfortunately, Clement did not examine the infra-red spectra of his materials so that their purities as *cis*-compounds are unknown. His and our melting point of erucone are in essential agreement and it may be that the disagreement as to the melting point of oleone is due to dimorphism.

We have also prepared these two ketones by condensing the methyl esters of the appropriate acids in a way which differed from that described by Clement mainly in convenience of procedure. Clement (1953*a*) showed that sodium hydride was most efficient if used together with small amounts of ethanol so that the stronger agent, sodium ethoxide, was formed in the reaction mixture. However, the sodium hydride also served to convert the ethanol arising from the condensation into sodium ethoxide, thereby suppressing reversal of the condensation. Sufficient sodium hydride was used to meet these two demands.

Briese and McElvain (1933) had earlier appreciated that for good yields of β-keto ester, and thence of ketone, reversal of the condensation must be suppressed by removal of the alcohol as formed, which they accomplished by reaction under reduced pressure at 125–130 °C. In the method now selected as convenient, the condensation was made in boiling xylene with sodium ethoxide as agent, allowing some xylene to distil during the reaction and to entrain the alcohol produced. The β-keto esters were not isolated and, without purification, were heated with alcoholic potash and the corresponding ketone isolated. In this way ketones were prepared from ethyl palmitate, ethyl undecylenate, methyl oleate, and methyl erucate ; none could be obtained from methyl 9,10-

dihydroxystearate. The four ketones prepared agreed in their properties with those already prepared by the method of Sauer.

The oleone and erucone prepared by Sauer's method on catalytic hydrogenation gave almost quantitative yields respectively of stearone and behenone; they were also readily elaidinized by sodium nitrite and dilute nitric acid to the corresponding *trans-trans*-ketones, elaidone and brassidone. For further characterization these four unsaturated ketones were oxidized by performic acid to the tetrahydroxy ketones. The oxidation is stereospecific. Oleone gave *threo*-9,10,26,27-tetrahydroxy-18-pentatriacontanone, m.p. 115 °C. Elaidone gave the *erythro*-9,10,26,27-tetrahydroxy-18-pentatriacontanone, m.p. 161–162 °C. Erucone gave *threo*-9,10,34,35-tetrahydroxy-22-tritetracontanone, m.p. 118 °C, and brassidone gave the corresponding *erythro*-compound, m.p. 154–155 °C.

The positions of the double bonds in oleone and elaidone were established by oxidation to 9-ketoheptadecanedioic acid, in one case directly by ozonization and in the other by oxidation of the first derived tetrahydroxy ketone with permanganate.

When these stereochemically pure unsaturated ketones were oxidized to the derived tetrahydroxy ketones or to 9-ketoheptadecanedioic acid, the products were readily obtained in good yield in a state of purity. This contrasted sharply with the behaviour of the products formed by similar oxidations of the liquid "oleone" produced by heating oleic acid with either iron filings or magnesium oxide. Oxidation with performic acid then failed to give a uniform product and on further oxidation a pure ketoheptadecanedioic acid could not be obtained. It must be concluded that ketonization of unsaturated acids at high temperatures is accompanied both by stereoisomeric change and by considerable migration of double bonds.

It was an aim of this work to explore the possibility of producing 9-ketoheptadecanedioic acid and thence large ring compounds, from oleic acid and the simple ketonization of the acid itself was an attractive feature of this route. Although for the satisfactory preparation of oleone it now appears to be necessary to proceed either through the ester or acid chloride, the preparation still compares in simplicity with the route from oleic acid through azelaic acid and ω-carbethoxycaprylyl chloride (Blomquist *et al.* 1952). By similar methods we have prepared from undecylenic acid first 1,20-heneicosadien-11-one and then from this 10-ketononadecanedioic acid.

A description of the isomeric ketones related to oleic and elaidic acids cannot be complete until the *cis-trans*-isomer is prepared. At present, work is in hand upon the synthesis of this compound and upon its isolation from elaidinized oleone, but the appearance of Clement's paper made it seem desirable to describe this first part of our work.

II. Experimental

Melting points are all corrected. Microanalyses were made by the C.S.I.R.O. Microanalytical Laboratory.

Oleic acid was obtained by saponification of olive oil and purified by low temperature crystallization of the distilled acids. Erucic acid from rape seed was purified by distillation of the methyl esters in a spinning band column. Elaidic and brassidic acids were prepared from the

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corresponding *cis*-acids by elaidinizing with dilute nitric acid and a little sodium nitrite, followed by recrystallization.

(*a*) *Oleone.*—The ketones were prepared by two methods: by the condensation of the corresponding acyl chloride in presence of triethylamine and by the alkaline condensation of the methyl or ethyl ester of the acid. The preparations of oleone by these two methods are given in detail and are typical, except that during the condensation of methyl oleate a gel-like condition developed in the reaction mixture which did not appear with the other esters. Probably for this reason the yield of oleone was low (30% theory). With the other ketones yields of 60–70% were readily obtained.

(i) *Method* (*1*) (cf. Sauer 1951). Oleic acid (iodine value, Wijs, 89·6; 9·8 g) was converted into its acyl chloride by heating with an excess of thionyl chloride in dry benzene. After freeing from solvent and thionyl chloride, the acyl chloride was dissolved in anhydrous ether (70 ml), cooled to 0 °C and triethylamine (3·6 g) added to the stirred solution during 10 min. After stirring 1 hr, the mixture was allowed to stand for 24 hr at room temperature, when the reaction mixture was first washed with 2% aqueous sulphuric acid to remove triethylamine and the ether then evaporated. The residue was refluxed (4 hr) with a 15% solution of potassium hydroxide in 90% ethanol and the crude ketone isolated by distilling part of the ethanol, adding water, and extracting it with light petroleum (b.p. 40–60 °C). After concentrating somewhat, this solution in light petroleum was chromatographed on alumina. The oleone was readily eluted by this solvent and, finally, was crystallized from acetone at 0 °C. It formed white crystals, m.p. 28–29 °C; iodine value, 100·8; yield 3·5 g (Found: C, 83·8; H, 13·2%. Calc. for $C_{35}H_{66}O$: C, 83·6; H, 13·2%).

(ii) *Method* (2). A solution of methyl oleate (14·8 g; 0·05 mol) in sodium-dried xylene (30 ml) was added to sodium ethoxide (0·025 mol from 0·6 g sodium) in xylene (70 ml). The mixture was heated at its b.p. and the alcohol, with some xylene allowed to distil from a short column attached to the reaction flask. After 6 hr, most of the xylene was distilled off and the residue was boiled under reflux for 3 hr with a 5% solution of potassium hydroxide in 90% ethanol (100 ml). Water was then added and the ketone extracted with light petroleum. The oleone was purified as described under Method (1). Again it melted at 28–29 °C.

The infra-red spectra of carbon disulphide solutions of oleone and elaidone were measured and by comparison the *trans*-impurity in the oleone was estimated to be 0·7% or less. Measured as a mull in "Nujol" oleone again showed no significant absorption at 964 cm^{-1}, the peak of the characteristic *trans*-band. The oleone (0·5 g) was hydrogenated in benzene-ethanol (1 : 1) using platinum oxide as catalyst and the product when crystallized from this medium formed white needles, m.p. 89 °C alone, or admixed with pure stearone (yield 0·4 g).

(*b*) *Elaidinization.*—Oleone (0·5 g) was suspended in dilute HNO_3 (HNO_3 (sp. gr. 1·4; 9 ml) and H_2O (21 ml)) and sodium nitrite (0·1 g) added. The oily layer solidified almost at once. After stirring and shaking for a few minutes at 40–50 °C, the product was washed with water and crystallized from acetone (yield 0·25 g). It melted at 73–74 °C alone or in admixture with pure elaidone.

(*c*) threo-*9,10,26,27-Tetrahydroxy-18-pentatriacontanone.*—A suspension of oleone (1 g) in formic acid (98%; 3 ml) and hydrogen peroxide (30%; 0·5 g) was stirred at 40 °C for 3 hr and the formic acid was then removed under reduced pressure. The remainder was heated with 10% aqueous sodium hydroxide for 1 hr on a steam-bath and the white crystalline product was filtered off, washed, and finally crystallized from ethyl acetate (yield 0·5 g). This tetrahydroxypentatriacontanone had m.p. 115 °C (Found: C, 73·6; H, 12·3%. Calc. for $C_{35}H_{70}O_5$: C, 73·6; H, 12·4%).

(*d*) *Oxidation to 9-Ketoheptadecanedioic Acid.*—*threo*-9,10,26,27-Tetrahydroxy-18-pentatriacontanone (0·8 g) dissolved in ethanol (40 ml) was mixed at 40 °C with potassium periodate (0·8 g) dissolved in sulphuric acid (1·0N; 42 ml), and after 10 min at 40 °C the solution was cooled and the products extracted with ether. The combined extracts, after washing and evaporation were steam distilled and the presence of nonanal in the distillate established by the preparation of its 2,4-dinitrophenylhydrazone (m.p. 104–105 °C after crystallization from ethanol).

The material not volatile in steam was extracted in ether and, after removal of this solvent, oxidized with potassium permanganate in acetone. The crude acid, isolated in the usual manner, and recrystallized from aqueous ethanol melted low (106 °C). It was purified by methylation in methanol solution with diazomethane and the ester, in light petroleum solution, chromatographed on alumina. The main fraction eluted by benzene, was saponified and the liberated acid when crystallized from benzene melted at 112–113 °C and at 112–114 °C when mixed with authentic 9-ketoheptadecanedioic acid.

(*e*) *Elaidone.*—This was prepared from elaidic acid according to the general procedure described above. It crystallized from acetone or from benzene-ethanol in colourless needles, m.p. 73–74 °C (Found: C, 83·3; H, 13·0%. Calc. for $C_{35}H_{66}O$: C, 83·6; H, 13·2%). Hydrogenation in benzene-ethanol (4 : 1), using a platinum oxide catalyst, gave stearone, m.p. 89 °C.

(*f*) erythro-*9,10,26,27-Tetrahydroxy-18-pentatriacontanone.*—Oxidation of elaidone with performic acid followed the method given for oleone except that during oxidation the temperature was held at 70–75 °C. The product crystallized rapidly when heated with sodium hydroxide solution. This tetrahydroxypentatriacontanone was sparingly soluble in hot ethanol, ethanol-benzene, and ethyl acetate. It was recrystallized from dioxan and then formed colourless needles, m.p. 161–162 °C (Found: C, 73·2; H, 12·4%. Calc. for $C_{35}H_{70}O_5$: C, 73·6; H, 12·4%).

(*g*) *Ozonolysis of Elaidone.*—The ketone (2 g) was ozonized in carbon tetrachloride (50 ml) and the product heated with a mixture of 5% aqueous NaOH (30 ml), and H_2O_2 (30 vol.; 2 ml) until solution was complete. After acidification with dilute sulphuric acid and removal of the volatile acids in steam, a solid acid remained in suspension. Collected and crystallized successively from aqueous ethanol and benzene it gave pure 9-ketoheptadecanedioic acid, m.p. 112–114 °C.

(*h*) *Erucone* (cis-cis-*9,34-Tritetracontadien-22-one*).—Erucone was prepared from erucic acid according to both general methods described for oleone. It crystallized from acetone in colourless needles, m.p. 50–51 °C (Found: C, 84·3; H, 13·6%. Calc. for $C_{43}H_{82}O$: C, 84·0; H, 13·4%). Hydrogenation of erucone gave 22-tritetracontanone ("behenone"), m.p. 96 °C, after crystallization from acetone. Backer and Strating (1940) report m.p. 96·0–96·3 °C (Found: C, 83·7; H, 13·9%. Calc. for $C_{43}H_{86}O$: C, 83·4; H, 14·0%).

(*i*) threo-*9,10,34,35-Tetrahydroxy-22-tritetracontanone* was prepared by oxidation of erucone with performic acid. It melted at 117–118 °C after crystallization from ethanol (Found: C, 75·7; H, 12·7%. Calc. for $C_{43}H_{86}O_5$: C, 75·6; H, 12·7%).

(*j*) *Brassidone* (trans-trans-*9,34-Tritetracontanone*).—Brassidone was prepared by Method (1) and also by elaidinization of erucone with nitric acid-nitrite by the method described for elaidone and repeated crystallization from acetone and finally from benzene-ethanol gave pure brassidone in colourless needles, m.p. 83–84 °C (Found: C, 84·3; H, 13·5%. Calc. for $C_{43}H_{82}O$: C, 84·0; H, 13·4%). Hydrogenation gave 22-tritetracontanone, m.p. 96 °C.

(*k*) erythro-*9,10,34,35-Tetrahydroxy-22-tritetracontanone* was obtained by performic acid oxidation of brassidone and was crystallized from dioxan. It melted at 154–155 °C (Found: C, 76·2; H, 12·8%. Calc. for $C_{43}H_{86}O_5$: C, 75·6; H, 12·7%).

(*l*) *Ketonization of Oleic Acid by Heating with Metallic Iron.*—Oleic acid (5 g) and iron powder (0·5 g) were heated at 330 °C under nitrogen for 2 hr. Vigorous frothing occurred during the reaction. The product was extracted with warm light petroleum and the dark extract chromatographed on alumina. The neutral material eluted by light petroleum did not all dissolve in hot acetone, but the acetone solution on cooling to 0 °C deposited a crystalline material which was crystallized repeatedly from this solvent. It then melted from 59 to 63 °C (Found: C, 83·5; H, 13·6%. Calc. for $C_{35}H_{66}O$: C, 83·6; H, 13·2%). As with oleone, the infra-red spectrum of this substance was compared with that of elaidone and the material thus estimated to contain 70% of *trans-trans*-isomers.

The oily product from such a ketonization when dissolved in benzene-ethanol and hydrogenated using a platinum oxide catalyst, readily gave stearone. After one recrystallization the product melted at 86 °C and the yield was 50% of theoretical. Oxidation of the oily product

with performic acid gave only an intractable mixture. Also elaidinization with nitric acid and nitrite did not give an easily purified elaidone, but a product which even after repeated crystallization from acetone melted at 65–70 °C.

(*m*) *1,20-Heneicosadien-11-one.*—Undecylenic acid was converted to the ketone by both general methods. This heneicosadienone crystallized from ethanol in needles, m.p. 49–50 °C (Found : C, 82·5 ; H, 12·5%. Calc. for $C_{21}H_{38}O$: C, 82·3 ; H, 12·5%).

(*n*) *11-Heneicosanone.*—This compound was obtained by hydrogenation of the above ketone in benzene-ethanol. After crystallization from methanol it had m.p. 63–64 °C. Breusch and Baykut (1953) give m.p. 63·5–64·5 °C (corr.) (Found : C, 81·4 ; H, 13·6%. Calc. for $C_{21}H_{42}O$: C, 81·2 ; H, 13·6%).

(*o*) *1,20-Heneicosadiene* was obtained by reduction of 1,20-heneicosadien-11-one by the Wolff-Kishner reduction in diethylene glycol. It was crystallized from acetone and had m.p. 33–34 °C (Found : C, 86·1 ; H, 14·1%. Calc. for $C_{21}H_{40}$: C, 86·2 ; H, 13·8%).

(*p*) *10-Keto-1,19-nonadecanedioic Acid.*—This acid was obtained from the above heneicosadienone by oxidation with permanganate in acetone (cf. Günthard, Heinemann, and Prelog 1953). The acid was converted to its *dimethyl ester* with diazomethane and purified by chromatography on neutral alumina (eluted by benzene but not by light petroleum). From light petroleum it separated in plates, m.p. 63–64 °C alone, or admixed with a sample of the ester prepared by ketonizing the acid chloride of the half-ester of sebacic acid (Found : C, 68·3 ; H, 10·4%. Calc. for $C_{21}H_{38}O_5$: C, 68·1 ; H, 10·3%).

III. Acknowledgments

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REDUCTION BY DISSOLVING METALS

XIII. THE PRODUCTION OF ALDEHYDES FROM AMIDINES, AMIDES, AND RELATED COMPOUNDS

By A. J. Birch,* J. Cymerman-Craig,* and M. Slaytor*

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Summary

The reduction by sodium and ethanol, with or without liquid ammonia as solvent, of various amidines followed by acid hydrolysis, leads in many cases to a good yield of the corresponding aldehyde. Further reduction in liquid ammonia of several 2-aryl-imidazolines or imidazolidines followed by acid hydrolysis leads to the 2,5-dihydro-benzaldehyde derivative.

The reduction of some acid amides by sodium and proton sources in liquid ammonia has been examined. Under the right conditions this process is of preparative value for aldehydes.

I. Aldehydes from Amidines

The ready availability of acids, nitriles, and amides makes any efficient process of converting them to aldehydes of value in synthesis. Among such methods are those due to Stephen (1925), Rosenmund and Zetzsche (1918), Sonn and Muller (1919), and McFadyen and Stevens (1936), all of which work well in some cases but are not of universal applicability. Recently (Birch, Hextall, and Sternhell 1954), the reduction of 2-phenylimidazoline with sodium and ethanol in liquid ammonia, followed by acid hydrolysis, was shown to produce benzaldehyde in 75 per cent. yield. Consequently we have now examined the reduction of the related amidines.

The reduction of amidines has been little investigated. Kirsanov and Polyakova (1936) reduced *N*-phenylbenzamidine with sodium amalgam and obtained a small amount of benzaldehyde, together with amines (see also Pyman 1923). Merling (1908) reduced some *NN'*-diphenylamidines with sodium and ethanol, and after acid treatment obtained about 80 per cent. yield of aldehyde from alicyclic amidines, but only 20–30 per cent. of benzaldehyde. The poor yield may be due to their method of working up the product. This kind of process, if improved and generalized, would be of use in synthesis since amidines can be readily prepared from nitriles, acids, and amides (e.g. Pinner 1883; Merling 1908; Oxley and Short 1947).

The mechanism of reduction is presumably that shown below (cf. Birch 1950). Probably the difference between the amidines and the oxygen analogues (esters) is due partly to the greater difficulty of reductive fission of C—N compared with C—O. Furthermore a *gem*-diamino group would be expected to show more stability under the alkaline conditions than one carrying an hydroxyl

* Department of Organic Chemistry, University of Sydney.

and either an alkoxyl or amino group on the same carbon, owing to the lower acidity of —NH— compared with —OH (see Section III). It is necessary to keep such a saturated group intact until the final acid hydrolysis, otherwise further reduction will occur.

$$RC{=}NH(NH_2) \xrightarrow{2\varepsilon} R\bar{C}{-}\bar{N}H(NH_2) \xrightarrow{2ROH} RCH(NH_2)_2$$
$$\xrightarrow{2H^+,\,H_2O} RCHO + 2NH_4^+.$$

On the basis of this mechanism the cationic amidine salts should be more readily reduced than the amidines themselves.

TABLE 1

REDUCTION OF SOME AMIDINES WITH SODIUM

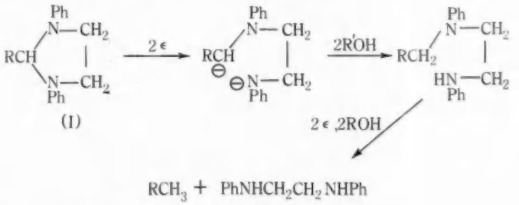
Amidine	Yield of Aldehyde (%)		Remarks
	Sodium-Alcohol	Sodium-Alcohol-Ammonia	
Benzamidine	97	100	
Benzamidine hydrochloride	—	100	
N-Phenylbenzamidine	54	91	
N-Ethylbenzamidine hydrochloride	—	100	
NN'-Diphenylbenzamidine	48	0	Insoluble in liquid ammonia
2-Phenylimidazoline	60	75	
Binziminoethyl ether hydrochloride	20–30*	7	
2-Phenylbenziminazole	0	0	
2-(*p-iso*Propylphenyl)imidazoline	—	100	
p-Methylsulphonylbenzamidine	31	—	Aldehyde obtained was benzaldehyde
p-Methylsulphonylbenzamidine hydrochloride		38	,, ,,
Acetamidine hydrochloride	—	55	Lower yields possibly due to solubility of 2,4-dinitrophenylhydrazone
Propionamidine hydrochloride	—	71	
n-Pentanecarboxamidine	—	91	
Glutarodiamidine dihydrochloride	—	53	
1,4'-Diphenylylamidino-*n*-hexadecane hydrochloride	—	0	Insoluble in liquid ammonia
1,4'-Diphenylylamidino*cyclo*hexane	—	74	
1,4'-Diphenylylamidino*cyclo*hexanebenzenesulphonate	—	27	Sparingly soluble in liquid ammonia
Phenylacetamidine	90	91	
Diphenylacetamidine	50	—	Low yield probably due to sensitivity to acids (in estimating aldehyde)

* Henle (1902).

The liquid ammonia method gave the better results when the compounds were soluble. The scale used was ~0·01M, the yield being estimated by formation of the 2,4-dinitrophenylhydrazones; the estimated yields are probably low for compounds giving fairly soluble derivatives (e.g. acetaldehyde) and for low molecular weight compounds which may be slightly volatile in boiling ammonia. No difficulty was experienced in isolating benzaldehyde on a larger scale in 70 per cent. yield from the reduction of *N*-ethylbenzamidine. The chief difficulty associated with the liquid ammonia process is the insolubility of some of the amidines. For this reason the *NN'*-unsubstituted compounds tend to give better yields. The imidazolines also seem to be particularly useful, probably because the intermediate 1,1-diamine structure is stabilized by being included in a ring.

II. Preparation of 2,5-Dihydrobenzaldehydes

One of the main problems in the reduction by metal-ammonia-alcohol solutions of aromatic rings is the protection of other reducible groups such as carbonyl. This can be accomplished in some cases by conversion to an acetal, provided the alkoxyl groups are not then in a benzyl position, or by conversion to an enol-ether if the resulting double bond is unconjugated. There are accordingly difficulties if the carbonyl group is α- or β- to an aromatic ring. A 2-arylimidazolidine is formally equivalent to an acetal with the oxygen atom replaced by —NH—, and with 2-phenylimidazolidine hydrogenolysis does not occur (Birch, Hextall, and Sternhell 1954). The reduction of 2-(*p-iso*propylphenyl)imidazoline followed by acid hydrolysis has now been investigated as a further example. 2,5-Dihydro-4-*iso*propylbenzaldehyde derivatives were obtained without isolation of the intermediates. This method, although it produces an aldehyde, is not a direct protection of the group, which arises through reduction of a group of higher oxidation level. We have accordingly examined the formation of imidazolidines directly from aldehydes.



Aldehydes, but not ketones, readily react with *NN'*-diphenyl or *NN'*-dibenzylethylenediamines to form the *NN'*-disubstituted imidazolidine (van Alphen 1935, 1936*a*, 1936*b*, 1938; Wanzlich and Lochel 1953). The presence of other reducible aromatic rings is in any case undesirable, and it is found that the *NN'*-diphenylimidazolidines undergo hydrogenolysis with sodium and ethanol in liquid ammonia: 2-(*p-iso*propylphenyl)-*NN'*-diphenylimidazolidine (I; R=$Me_2CHC_6H_4$) gave only a hydrocarbon product, presumably 2,5-dihydro-1-methyl-4-*iso*propylbenzene. On the basis of the type of mechanism already outlined (Birch 1950; Birch, Hextall, and Sternhell 1954) this hydrogenolysis

probably occurs in two successive stages as shown on p. 514, the energy level of the negative charge on the nitrogen being lowered by resonance with the attached phenyl group.

To avoid hydrogenolysis the non-aromatic amine, *NN'*-dimethylethylenediamine, was used. This readily condensed with benzaldehyde, and the imidazolidine was reduced without isolation. The final product after acid hydrolysis was 2,5-dihydrobenzaldehyde (60 per cent.) isolated as the semicarbazone. This diamine is therefore a direct protecting reagent for aldehyde groups, and further applications are under investigation.

TABLE 2

REDUCTIONS WITH SODIUM-ETHANOL-AMMONIA

Amide	Aldehyde	Yield (%)
N-Ethylbenzamide	Benzaldehyde	0
NN'-Diethylbenzamide	,,	7
N-Methyl-*N*-phenylbenzamide	,,	14
Benzoylpiperidide	,,	28
NN'-Diethylhexanoamide	Hexanoic aldehyde	0
N-Methyl-*N*-phenylhexanoamide	,, ,,	23
Hexanoylpiperidide	,, ,,	3, 9

III. ALDEHYDES FROM AMIDES

The only reductions of amides by dissolving metal reagents to give aldehydes are recorded by Clemo and King (1948), who obtained an aldehyde from strychnine with sodium and ethanol in liquid ammonia and acetaldehyde from

TABLE 3

EFFECT OF PROTON SOURCES ON YIELD OF ALDEHYDES

Amide	Proton Source	Aldehyde Yield (%)
Benzoylpiperidide	Ethanol	28
,,	Water	46
,,	Phenol	56
,,	Acetic acid	80
,,	Ammonium chloride	48
N-Methyl-*N*-phenylhexanoamide	Ethanol	23
N-Methyl-*N*-phenylhexanoamide	Acetic acid	53
N-Methyl-*N*-phenyl*cyclo*hexanecarboxamide	Acetic acid	47

N-methylacetanilide. Other amides were stated to give little, if any aldehyde. We have confirmed that under these conditions only low yields are usually obtained (Table 2). It was noted that nitrogen-free products were obtained from the acyl portion of the molecule. The stability of the cyclic strychnine

derivative is suggestive, and the removal of nitrogen is explicable on the basis of the mechanism below, the desired intermediate II being decomposed, because of the alkaline conditions, to give the aldehyde which is further reduced. Accordingly stronger "acids" than ethanol were used to inhibit the base-catalysed fission and much higher yields were obtained (Table 3). An additional advantage of the use of proton donors, such as acetic acid (ammonium acetate), is that benzene rings are then unaffected by excess reducing agent (Birch, unpublished data). The lower yield with ammonium chloride, which is a strong acid of the ammonia system, may be due to an acid-catalysed decomposition of II, through the conjugate acid.

Recently lithium aluminium hydride has been used to reduce amides to give eventually aldehydes in good yield (Mousseron *et al.* 1952; Micovic and Mihailovic 1953; Weygand *et al.* 1953). In some instances the present procedure which is rapid, cheap, and simple may be superior.

$$R{-}C{=}O(NR'_2) \xrightarrow[2R''OH]{2Na} \underset{(II)}{R{-}CHOH(NR'_2)} + 2NaOR'' \rightleftharpoons R{-}\underset{\downarrow}{CHONa(NR'_2)} + R''OH$$

$$\text{reduction products} \longleftarrow R{-}CHO + HNR'_2 + R''ONa.$$

A preliminary note on some of this work has been published elsewhere (Birch, Cymerman-Craig, and Slaytor 1954).

IV. Experimental

(*a*) *Preparation of Amidines.*—These were prepared by standard methods, the hydrochlorides being basified with aqueous sodium hydroxide (40%) and the base extracted with chloroform.

(*b*) *Reductions A: Amidines with Sodium and Ethanol.*—To the base (0·0057 mole) in absolute ethanol (60 c.c.) was added under reflux sodium (3·5 g) gradually in small pieces. After completion of the reaction, the mixture was diluted with water (30 c.c.) and acidified to congo paper with concentrated hydrochloric acid. Somewhat more than an equivalent of 2,4-dinitrophenylhydrazine was then added in solution in ethanol-sulphuric acid. The derivative was filtered, washed, and dried. The benzaldehyde derivative obtained from the various preparations melted at temperatures between 231 and 237 °C.

p-*Methylsulphonylbenzamidine*, m.p. 187 °C (hydrochloride, m.p. 294 °C) (Found: C, 47·9; H, 4·9%. Calc. for $C_8H_{10}O_2N_2S$: C, 48·5; H, 5·1%) gave benzaldehyde 2,4-dinitrophenylhydrazone, m.p. 231 °C (Found: C, 54·5; H, 3·7%. Calc. for $C_{13}H_{10}O_4N_4$: C, 54·5; H, 3·5%). Phenylacetamidine produced phenylacetaldehyde 2,4-dinitrophenylhydrazone as yellow plates, m.p. 122 °C, undepressed by an authentic specimen.

Diphenylacetamidine was an oil, characterized as the *picrate*, m.p. 210 °C (Found: C, 54·5; H, 3·8%. Calc. for $C_{20}H_{17}O_7N_5$: C, 54·7; H, 3·9%). The crude *diphenylacetaldehyde 2,4-dinitrophenylhydrazone* was rather dark in colour, probably due to the great sensitivity of the aldehyde. It crystallized as light orange plates from benzene-ethanol, m.p. 152 °C (Found: C, 63·9; H, 4·2%. Calc. for $C_{20}H_{16}O_4N_4$: C, 63·8; H, 4·3%).

(*c*) *Reduction B: Amidines with Sodium and Ethanol in Ammonia.*—The base or its hydrochloride (0·01 mole) was dissolved in ethanol (10 c.c.) and added to liquid ammonia (100 c.c.). Sodium was then added gradually in small pieces (aliphatic amidines 0·026 mole, aromatic amidines 0·021 mole). Two methods were used to work up the aldehydes: (i) after completion of the reduction, water (50 c.c.) was added and the *gem*-diamine extracted with ether (3 × 100 c.c.). The extract was dried with potassium carbonate and the ether removed, leaving an unpleasant smelling oil. In the case of the imidazolines this oil crystallized but was not successfully purified

owing to instability. Reaction with 2,4-dinitrophenylhydrazine as above gave the derivative. (ii) After evaporation of the ammonia the solution was acidified to 2N with hydrochloric acid and reacted directly as above with 2,4-dinitrophenylhydrazine.

This method gave better results than (1) with low mol. wt. compounds, e.g. propionamidine, the diamines from which are volatile in ether.

A larger-scale reduction of *N*-ethylbenzamidine (10 g) using the proportions above gave benzaldehyde (5·1 g), b.p. 70 °C/15 mm; 2,4-dinitrophenylhydrazone, m.p. 237 °C.

The following 2,4-dinitrophenylhydrazones were obtained in the yields stated in Table 1: acetaldehyde, m.p. 165 °C; propionaldehyde, m.p. 150 °C; hexanal, m.p. 98 °C; *glutaro-dialdehyde* (*bis-derivative*), m.p. 185 °C (Found: C, 44·3; H, 3·6%. Calc. for $C_{17}H_{16}O_8N_8$: C, 44·4; H, 3·5%); formyl*cyclo*hexane, m.p. 170 °C; cuminaldehyde, m.p. 240 °C.

(*d*) *Reduction of 2-*(p-iso*Propylphenyl*)*-1,3-diphenylimidazolidine.*—4-*iso*Propylbenzaldehyde (3·9 g) was heated to 60 °C for 2 min in admixture with 1,4-dianilinoethane (5·3 g), acetic acid (1·1 c.c.), and methanol (100 c.c.). After leaving for 12 hr the 2-(*p-iso*propylphenyl)-1,3-diphenylimidazolidine had crystallized and was recrystallized from light petroleum (b.p. 40–70 °C), m.p. 122 °C (Found: N, 8·2%. Calc. for $C_{24}H_{26}N_2$: N, 8·2%).

The above imidazolidine (15 g) in ethanol (25 c.c.) and tetrahydrofuran (sufficient to complete solution) was added to liquid ammonia (400 c.c.) and to this was added sodium (12·6 g) in small pieces. After reaction was complete, water (50 c.c.) was added, the product extracted with ether, washed with acid, and distilled, b.p. 98 °C/50 mm n_D^{19} 1·4808. It was essentially a dihydro-*p*-cymene, probably γ-terpinene (Found: C, 87·5; H, 11·6%. Calc. for $C_{10}H_{16}$: C, 88·15; H, 11·8%).

(*e*) *Reduction of 1,3-Dimethyl-2-phenylimidazolidine.*—Benzaldehyde (1 mole) was mixed with *NN*-dimethylethylenediamine (1 mole) the mixture becoming warm. Light petroleum (b.p. 60–90 °C) was added, followed by anhydrous potassium carbonate to remove water. Removal of the solvent under reduced pressure left an oil with an unpleasant odour.

The crude imidazolidine (1 g) in ethanol (10 c.c.) and ammonia (100 c.c.) was reduced by the addition of sodium (1 g). The product worked up as above was extracted from the acidified solution and converted to the semicarbazone (0·58 g, 60%), m.p. 206 °C undepressed by the authentic derivative of 2,5-dihydrobenzaldehyde (Birch, Hextall, and Sternhell 1954).

(*f*) *Reduction of 2-*(p-iso*Propylphenyl*)*imidazoline.*—4-*iso*Propylbenzonitrile (65 g) and ethylenediamine mono-*p*-toluenesulphonate (65 g) were heated to 200 °C until ammonia was no longer evolved (3·5 hr). After cooling, the product was dissolved in water, extracted with benzene, basified to phenolphthalein with 10N sodium hydroxide, and the imidazoline extracted with chloroform. After removal of the solvent the residue was crystallized from light petroleum (b.p. 60–90 °C) to give *2-*(p-iso*propylphenyl*)*imidazoline* (yield 36 g, 64%) as colourless plates, m.p. 106–107 °C (Found: C, 76·7; H, 8·9%. Calc. for $C_{12}H_{16}N_2$: C, 76·6; H, 8·5%).

The imidazoline (5 g) in ethanol (25 c.c.) and ammonia (500 c.c.) was reduced by the addition of sodium (9·5 g). Water (100 c.c.) was then added and the product extracted with ether. The resulting imidazolidine was a low-melting solid which was not purified, but was converted directly to the derivatives of 2,5-dihydro-4-*iso*propylbenzaldehyde.

The *semicarbazone* was obtained by the action in the cold of aqueous semicarbazide hydrochloride; it formed colourless needles from aqueous ethanol, m.p. 196 °C (Found: C, 63·8; H, 8·0%. Calc. for $C_{11}H_{17}ON_3$: C, 63·7; H, 8·2%). The ultraviolet spectrum had maximum absorption at 264 mμ, ε 24,200, in accord with that to be expected from an αβ-unsaturated aldehyde derivative. The 2,4-*dinitrophenylhydrazone* was obtained by the action of Brady's reagent as fine red needles, m.p. 199 °C (Found: C, 58·1; H, 5·4%. Calc. for $C_{16}H_{18}O_4N_4$: C, 58·2; H, 5·5%).

(*g*) *Reduction of Amides.*—The amides were prepared according to the Schotten-Baumann method. *N-Methyl-N-phenylhexanoamide* had b.p. 97 °C/0·01 mm, n_D^{25} 1·5095 (Found: C, 75·9; H, 9·5%. Calc. for $C_{13}H_{19}ON$: C, 76·1; H, 9·3%); *hexanoylpiperidide* had b.p. 116–118 °C/5 mm, n_D^{23} 1·4770 (Found: C, 72·2; H, 11·4%. Calc. for $C_{11}H_{21}ON$: C, 72·1;

H, 11·5%); N-*methyl*-N-*phenyl*cyclo*hexanecarboxamide* had m.p. 63 °C (Found: C, 76·9; H, 8·8%. Calc. for $C_{14}H_{19}ON$: C, 77·4; H, 8·8%).

The amide (0·01M) was dissolved in the proton source (slightly more than theoretically required) and added to liquid ammonia (70 c.c.). Sodium (0·021M) was added in small pieces. When the sodium had reacted the ammonia was evaporated and the mixture acidified to congo paper with dilute hydrochloric acid. The 2,4-dinitrophenylhydrazone was prepared as above. A larger-scale experiment was carried out similarly on benzoylpiperidide (18·9 g). The acidified solution was extracted with ether and distilled to give benzaldehyde (8·2 g, 68%), b.p. 70 °C/15 mm, 2,4-dinitrophenylhydrazone, m.p. 235 °C.

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HYDROAROMATIC STEROID HORMONES

IV. (+)-19-NOR-D-HOMOTESTOSTERONE

By A. J. BIRCH* and R. J. HARRISSON*

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Summary

(+)-19-Nor-D-homotestosterone (III) has been synthesized by reduction of (+)-D-homo-oestrone methyl ether with lithium and ethanol in liquid ammonia, followed by acid hydrolysis.

I. INTRODUCTION

In a survey of possible substitutes for steroid hormones (Birch 1950*a*), the conclusion was reached that 19-norsteroids should be biologically active and that 18-norsteroids might be active if ring D were six-membered. Confirmation was obtained by demonstrating the androgenic activity of (+)-19-nortestosterone (Birch 1950*b*), which was in fact the first androgen to be made by total synthesis. Later other 19-norsteroids were shown to be biologically active by Djerassi, Miramontes, and Rosenkranz (1953), Djerassi *et al.* (1953, 1954, 1955). Johnson, Lemaire, and Pappo (1953) found that (±)-18-nor-D-homoandrostan-3,17*a*-dione is as active an androgen as the analogous true steroid (+)-androstan-3,17-dione. Disappointingly, however, (±)-18,19-bisnor-D-homotestosterone was found to be inactive (Johnson, Dehm, and Chinn 1954) although some evidence is available that an 18,19-bisnor-D-homosteroid may possess some activity (Birch and Quartey 1953). The limits of structural alteration are therefore still not clear, and it is not certain that 18,19-bisnor-D-homosteroid analogues of other hormones will be inactive since androgenic activity is apparently highly structure-specific. Moreover, other types of activity, for example, anabolic activity, might still be present. 19-Nortestosterone has only about 30 per cent. of the androgenic activity of testosterone but has about 70 per cent. of the anabolic activity.

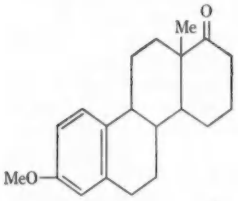
II. (+)-19-NOR-D-HOMOTESTOSTERONE

The synthesis of (+)-19-nor-D-homotestosterone (III) is desirable in order to test the biological effect of retaining the 18-methyl group in a structure which is inactive without it. The *cyclo*hexenone A-ring was prepared from an aromatic A-ring by the same type of process as that used for making 19-nortestosterone from oestrone ethers (Birch and Mukherji 1949; Birch 1950*a*) and extended to the other 19-norsteroids (Djerassi, Miramontes, and Rosenkranz 1953; Djerassi *et al.* 1953, 1954, 1955).

* Department of Organic Chemistry, University of Sydney.

(+)-D-Homo-oestrone methyl ether (I) was prepared by the expansion of ring D of (+)-oestrone methyl ether using the method of Heusser *et al.* (1950). Preliminary reduction to D-homo-oestradiol methyl ether was carried out by sodium borohydride. The resulting compound should on general grounds be the 17αβ-hydroxy compound (e.g. Cram and Abd Elhafez 1952) having the natural configuration.

Reduction of the aromatic A-ring was carried out by the modification of the metal-ammonia-ethanol method employing lithium (Wilds and Nelson 1953) to give the dihydro-derivative II. Hydrolysis with hot 1N hydrochloric acid in ethanol gave rise to (+)-19-nor-D-homotestosterone (III). The biological investigation of this substance will be reported elsewhere.



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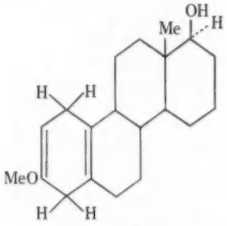

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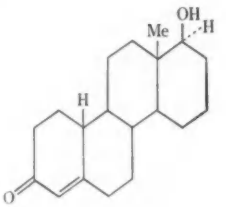

(III)

III. Experimental

(*a*) D-*Homo-oestrone Methyl Ether.*—To (+)-oestrone methyl ether (1·1 g) in ethanol (35 c.c.) and potassium cyanide (6 g) cooled at 0 °C was added acetic acid (6·4 c.c.). After stirring for 1 hr at 0 °C and 2·5 hr at room temperature the reactants dissolved and potassium acetate precipitated. Water (65 c.c.) was added, the precipitated solid filtered, taken up in ethyl acetate, the solution washed with water, dried, and evaporated. The pure *17α-cyano-17β-hydroxy-3-methoxyoestrane* could be obtained as needles, m.p. 158·5 °C (sealed tube) after several crystallizations from *cyclo*hexane-acetone (Found : C, 76·8 ; H, 8·0%. Calc. for $C_{20}H_{25}O_2N$: C, 77·1 ; H, 8·1%).

The crude cyanohydrin was taken up in pyridine (15 c.c.) and acetic anhydride (15 c.c.) and left at room temperature for 52 hr. The excess reagents were evaporated under reduced pressure below 60 °C and the residue taken up in ether, washed with acid, then water, dried, and crystallized from *cyclo*hexane containing 5–10% of acetone as massive prisms (0·9 g), m.p. 130–132 °C. The mother liquor was chromatographed on alumina (10 g), eluting with *cyclo*hexane-benzene (10 : 1) in 50 c.c. fractions. The first fractions gave regenerated oestrone methyl ether (30 mg), m.p. 162–165 °C ; the later fractions eluted with *cyclo*hexane-benzene (3 : 2) gave the desired acetyl derivative (80 mg), m.p. 125–128 °C, and finally some unacetylated cyanohydrin (30 mg), m.p. 156–160 °C. The combined *17β-acetoxy-17α-cyano-3-methoxyoestrane* was recrystallized from *cyclo*hexane-acetone and had m.p. 133 °C. The analytical specimen was sublimed at 120 °C/10^{-4} mm, m.p. 133 °C (Found : C, 74·4 ; H, 7·7%. Calc. for $C_{22}H_{27}O_3N$: C, 74·8 ; H, 7·7%).

The above acetyl compound (1·8 g) in benzene (75 c.c.) and ether (75 c.c.) was added dropwise at 0 °C to lithium aluminium hydride (3·5 g) in ether (300 c.c.). After stirring for 1 hr the mixture was refluxed for 1·5 hr. Water (100 c.c.) was carefully added, the organic solvents were directly evaporated, and to the aqueous solution was added sodium hydroxide solution (100 c.c. ; 10%). The solid was filtered, washed, dried, powdered, and extracted in a Soxhlet with acetone for 8 hr. The acetone was evaporated, finally, under reduced pressure, the product was taken up in aqueous acetic acid (100 c.c. ; 5%), washed with ether, and basified with aqueous sodium hydroxide (10%). The amorphous solid was removed by filtration and dried (1·56 g),

m.p. 160–162 °C. The *17α-aminomethyl-17β-hydroxy-3-methoxyoestrane* was purified for analysis by vacuum sublimation at 140 °C/0·1 mm, m.p. 163 °C (Found : C, 76·0 ; H, 9·3%. Calc. for $C_{20}H_{29}O_2N$: C, 76·2 ; H, 9·3%).

To a solution of the amine (1·5 g) in acetic acid (10 c.c.) and water (200 c.c.) at 0 °C was added slowly sodium nitrite (0·492 g) in water (20 c.c.). The reaction mixture was stirred at 0 °C for 3 hr and left at room temperature for 24 hr. The precipitated product was removed by filtration and crystallized from ethanol to give D-homo-oestrone methyl ether (1·0 g), m.p. 131–134 °C. Goldberg and Studer (1941) give m.p. 138·5–139·5 °C.

(*b*) *D-Homo-oestradiol Methyl Ether.*—D-Homo-oestrone methyl ether (0·9 g) in ethanol (120 c.c.) was added to a solution of sodium borohydride (0·4 g) in water (5 c.c.) and ethanol (60 c.c.). The mixture was left overnight and acidified with dilute hydrochloric acid. The ethanol was removed under reduced pressure, the residue taken up in ether, washed, and dried. After removal of the solvent the residue crystallized on contact with aqueous methanol to give crystals (0·87 g), m.p. 72–76 °C. Several crystallizations from aqueous methanol gave *17aβ-hydroxy-3-methoxy-D-homo-oestrane*, m.p. 93·5–94·5 °C (Found : C, 79·6 ; H, 9·5%. Calc. for $C_{20}H_{32}O_2$: C, 80·0 ; H, 9·4%) $[\alpha]_D$ + 101·5° (chloroform).

(*c*) *1,4-Dihydro-17aβ-hydroxy-3-methoxy-D-homo-oestrane.*—The above compound (1·48 g) in dry ether (135 c.c.) was added rapidly to liquid ammonia (175 c.c.) and to the turbid stirred solution was added lithium (1·75 g) over 1 min period. The resulting solution was stirred for 15 min and ethanol (20 c.c.) added over 15–20 min, the colour being discharged at about 15 c.c. addition. The ammonia was evaporated and water (75 c.c.) added. The ether extracted product was crystallized from absolute ethanol-light petroleum (b.p. 60–80 °C ; 1 : 5) as colourless needles (0·85 g), m.p. 115–118 °C. The mother liquors gave a further crop (0·15 g), m.p. 105–111 °C. Several crystallizations from light petroleum (b.p. 60–90 °C) gave *1,4-dihydro-17aβ-hydroxy-3-methoxy-D-homo-oestrane*, m.p. 115–117 °C. For analysis the substance was dried for 30 hr at 50 °C/0·5 mm (Found : C, 79·5 ; H, 9·9%. Calc. for $C_{20}H_{30}O_2$: C, 79·4 ; H, 10·0%). The substance is not very stable and on leaving the m.p. falls.

The substance (370 mg) in methanol (30 c.c.) and oxalic acid (0·46 g) in water (26 c.c.) were shaken for 40 min. Water was added, the product taken up in ether, well washed with sodium bicarbonate solution and water, dried, and evaporated. Crystallization from ethyl acetate gave what is probably essentially 17*aβ*-hydroxy-3-keto-D-homo-19-norandros-5(10)-ene (160 mg), m.p. 117–134 °C, $\lambda_{max.}$ 285 mμ, $\varepsilon_{max.}$ 93. After chromatography on neutral alumina in benzene the initial fractions were gummy, and the final fraction gave a solid, m.p. 138–143 °C, $\lambda_{max.}$ 238 mμ, $\varepsilon_{max.}$ 9400 ; giving rise to a *2,4-dinitrophenylhydrazone* as bright red needles, m.p. 225·5–226·5 °C (Found : C, 64·2 ; H, 6·9 ; N, 12·1%. Calc. for $C_{25}H_{32}O_5N_4$: C, 64·1 ; H, 6·9 ; N, 12·0%). Several crystallizations of the ketone from benzene-light petroleum (b.p. 60–90 °C) gave needles, m.p. 156–157 °C, insufficient for analysis. It is apparent that alteration has occurred on chromatography. The crystalline compound is not identical with the desired product described below.

Direct hydrolysis to *19-nor-D-homotestosterone* was accomplished as follows. The ether (120 mg) in methanol (3 c.c.) and 1N hydrochloric acid (3 c.c.) was maintained at 60 °C for 15 min, cooled, and diluted with water. The solid (85 mg) was removed by filtration and crystallized three times from light petroleum (b.p. 60–90 °C)-benzene to give the desired compound as as colourless prisms, m.p. 128 °C (Found : C, 79·3 ; H, 9·8%. Calc. for $C_{19}H_{28}O_2$: C, 79·1 ; H, 9·8%), $\lambda_{max.}$ 241·5 mμ, $\varepsilon_{max.}$ 17,000.

IV. Acknowledgments

We are indebted to the National Health and Medical Research Council for the financial support of this work.

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BARBALOIN

I. SOME OBSERVATIONS ON ITS STRUCTURE

By A. J. Birch* and F. W. Donovan*

[*Manuscript received April* 15, 1955]

Summary

The reactions of barbaloin are shown to be consistent with the formula $C_{21}H_{24}O_9$. It is suggested on the basis of absorption spectra and published data that the molecule contains an aloe-emodinanthrone ring system which cannot enolize to form the anthranol.

I. Introduction

Barbaloin, the principal purgative substance from Barbados aloes, has been extensively but inconclusively investigated over the past 60 years. There is little to be gained from a summary of the confused literature since most of it is based on incorrect empirical formulae. In a brief note Owen and Simonsen (1942) proposed the formula $C_{21}H_{24}O_9$ on the basis of the molecular weight of the heptamethyl ether determined by X-ray analysis. Although this conclusion has been stated (Gardner 1945) to be in harmony with the analyses of many of the derivatives of barbaloin there has been no general consideration of the problem based on this formula. The principal conclusions regarding reasonably well-defined derivatives of barbaloin which emerge from such a reinterpretation are shown in Table 1.

II. Degradations of Barbaloin

The principal degradations lead to derivatives of aloe-emodinanthrone (I) or aloe-emodin, together with (+)-arabinose and formaldehyde or methanol (Leger 1916 ; Cahn and Simonsen 1932 ; Hauser 1931 ; Gardner and Campbell 1942). Under some conditions furfural replaces the arabinose. Gardner (1945) has suggested that formaldehyde and furfural can arise from a C_6-sugar, but it seems preferable to believe that barbaloin contains a nucleus of the type I with attached C_1 and C_5 chains. Most formulae hitherto proposed have been glycosides of aloe-emodin or aloe-emodinanthrone. Barbaloin is however unlikely to be an ordinary arabinoside, because arabinose is not produced by the methods of hydrolysis usually successful in this series (Gardner, McDonnell, and Wiegand 1934 ; Foster and Gardner 1936), the method employed being acid hydrolysis in the cold for 6 months (Leger 1916).

The formation of arabinose may be due to the fission of a carbon-carbon link by a reverse-aldol reaction in a formula such as II. Alternatively, arabinose might be formed by the oxidation of a pentahydroxypentane, during hydrolysis

* Department of Organic Chemistry, University of Sydney.

TABLE 1

DERIVATIVES OF BARBALOIN

Derivative	Preparation	Calc. for Formula (%)	Analysis Found (%)	Reference
A. Heptamethyl	MeI and Ag_2O	$C_{21}H_{17}O_3(OMe)_7$ C, 64·9; H, 7·3; OMe, 41·9	C, 64·5; 64·7; 64·3; OMe, 40·7 H, 7·2; 7·1; 7·1 C, 65·4; H, 7·2; OMe, 41·4	Cahn & Simonsen (1932) Present work
B. Dibenzoyl- or tribenzoyl-	Benzoyl chloride in pyridine	$C_{21}H_{22}O_7(OCOC_6H_5)_2$ C, 66·9; H, 5·1	C, 67·6; 67·3 H, 5·1; 4·9	Leger (1916)
C. Pentabenzoyl-	Benzoyl chloride at 100 °C on *B*	$C_{21}H_{19}O_4(OCOC_6H_5)_5$ C, 71·5; H, 4·7	C, 70·8; H, 4·9	Leger (1916)
D. Hepta-acetyl-	Acetic anhydride-NaAc at 100 °C	$C_{21}H_{17}O_3(OAc)_7$ C, 58·8; H, 5·3 Ac, 42·0	C, 58·6; H, 5·4 Ac, 35·9 Ac, 41·6	Tilden (1875) Leger (1916) Present work
E. Tribromo-	Br_2-HBr	$C_{21}H_{21}O_9Br_3$ C, 38·4; H, 3·2; Br, 36·5	C, 38·4; H, 3·4; Br, 36·5 C, 37·7; H, 3·0; Br, 37·8; 37·6	Leger (1916) Gibson & Simonsen (1930)*
F. Hexa-acetyl-	Ac_2O on *E*	$C_{21}H_{15}O_3Br_5(OAc)_6$ C, 43·5; H, 3·6; Br, 26·4	C, 43·4; H, 3·5; Br, 26·4	Gibson & Simonsen (1930)*
G. Pentamethyl-tribromo-	Me_2SO_4-KOH on *E*	$C_{21}H_{16}O_4Br_3(OMe)_5$ C, 42·9; H, 4·3; Br, 33·0; OMe, 21·3	C, 43·0; H, 4·0; Br, 33·3; OMe, 22·9	Gibson & Simonsen (1930)*
H. Acetylpenta-methyltribromo-	Ac_2O on *G*	$C_{21}H_{15}O_3Br_3(OMe)_5(OAc)$ C, 43·7; H, 4·3; Br, 31·2; Ac, 5·6	C, 44·1; H, 4·1; Br, 31·4; Ac, 6·4	Gibson & Simonsen (1930)*

* A number of authors give much the same results as the references cited.

TABLE 1 (*Continued*)

Derivative	Preparation	Calc. for Formula (%)	Analysis Found (%)	Reference
I. Tetrabromo-	Br_2-H_2O	$C_{21}H_{20}O_5Br_4$	C, 35·5; H, 2·8; Br, 42·0	A number of authors gave much the same results as the references cited
		C, 34·2; H, 2·7; Br, 43·4	C, 34·1; H, 2·9; Br, 42·9	Jowett & Potter (1905)
			Br, 42·6	Gibson & Simonsen (1930)*
			Br, 41·8; 43·1	Leger (1916)
J. Penta-acetyl-tetrabromo-	AcCl on *I*	$C_{21}H_{15}O_4Br_4(OAc)_5$	C, 39·0; H, 3·1; Br, 33·4	Jowett & Potter (1905)
		C, 39·3; H, 3·2; Br, 33·8; Ac, 22·7	Br, 32·5; Ac, 24·0	Gibson & Simonsen (1930)*
K. Hepta-acetyl-tetrabromo-	Ac_2O-H_2SO_4 on *I*	$C_{21}H_{13}O_2Br_4(OAc)_7$ C, 40·7; H, 3·3; Br, 31·1	C, 40·5; H, 3·0; Br, 31·0	Gibson & Simonsen (1930)*
L. Hexamethyl-tetrabromo-	Me_2SO_4-KOH on *I*	$C_{21}H_{14}O_5Br_4(OMe)_6$	C, 39·5; H, 3·6; Br, 38·6; OMe, 21·4	Gibson & Simonsen (1930)*
		C, 39·3; H, 3·9; Br, 38·7; OMe, 22·5	C, 40·1; H, 3·9; Br, 37·8	
M. Tetramethyl-tetrabromo-	Piperidine at 100 °C on *L*	$C_{21}H_{16}O_5Br_4(OMe)_4$	C, 38·2; H, 3·5; Br, 39·8; OMe, 15·4	Cahn & Simonsen (1932)
		C, 37·9; H, 3·5; Br, 40·4; OMe, 15·7	C, 38·4; H, 3·4; Br, 39·6; OMe, 13·4	
N. Tetrachloro-	Cl_2-HCl	$C_{21}H_{20}O_5Cl_4$ C, 45·2; H, 3·6; Cl, 25·4	C, 45·9; H, 3·45; Cl, 24·9, 25·1	Leger (1916)
O. Penta-acetyl-tetrachloro-	AcCl on *N*	$C_{21}H_{15}O_4Cl_4(OAc)_5$ C, 48·4; H, 3·9; Cl, 18·5	C, 48·2; H, 4·1; Cl, 18·8, 18·5	Leger (1916)

* A number of authors give much the same results as the references cited.

under oxidizing conditions. A possible formula on the evidence below is IV. The presence of such blocked anthrone structures can be tested by seeing whether the carbonyl group is capable of giving enol (anthranol) derivatives.

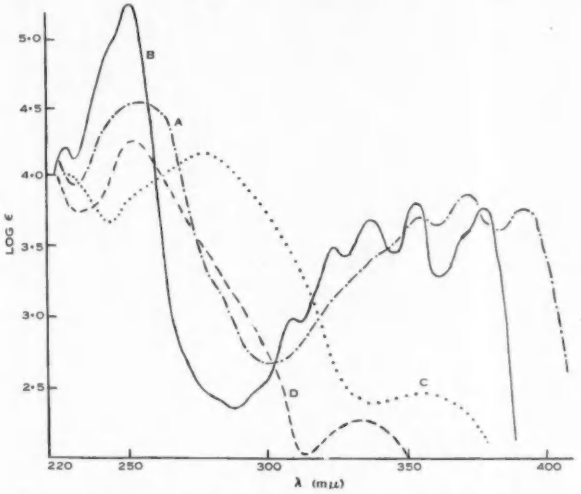


Fig. 1.—*A*, tetra-acetylbarbaloin (ethanol); *B*, anthracene (hexane); *C*, hepta-acetylbarbaloin (ethanol); *D*, benzophenone (ethanol).

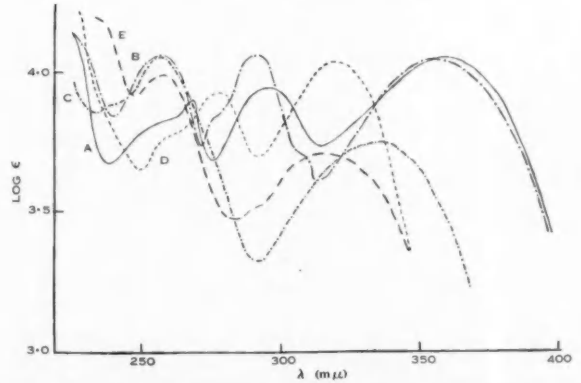
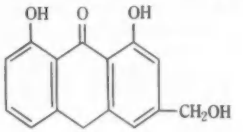


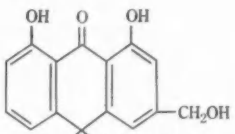
Fig. 2.—*A*, barbaloin (ethanol); *B*, aloe-emodinanthrone (ethanol); *C*, 2,2′-dihydroxybenzophenone (ethanol); *D*, heptamethylbarbaloin (ethanol); *E*, 2,2′-dimethoxybenzophenone (ethanol).

Aloe-emodinanthrone (I), for example, readily gives the tetra-acetate (III). The ultraviolet spectrum of III (Fig. 1, curve *A*) is similar to that of anthracene (Fig. 1, curve *B*) in accord with the known fact that acetylation of an

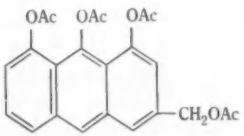
hydroxyl group nearly or completely cancels its action on an attached chromophore. The spectrum (Fig. 1, curve *C*) of hepta-acetylbarbaloin, now prepared pure for the first time, differs completely and resembles that of benzophenone (Fig. 1, curve *D*) and the closely similar 2,2′-diacetoxybenzophenone (not shown) although there is displacement to longer wavelengths. Barbaloin and aloe-emodinanthrone are similar (Fig. 2, curves *A* and *B*) with some differences at lower wavelengths. They differ from 2,2′-dihydroxybenzophenone (curve *C*) not only in displacement of the longer-wavelength band, but also in the appearance of a new band at 290–295 mμ. They demonstrate the closeness in structure of the chromophores in these substances. Heptamethylbarbaloin (Fig. 2, curve *D*) is similar to 2,2′-dimethoxybenzophenone (Fig. 2, curve *E*) if it is assumed that another middle peak is present and that the inflexion at about 260 mμ is equivalent to the peak in curve *E* at 260 mμ.



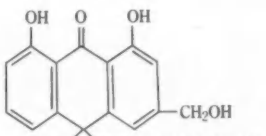
(I)



(II)



(III)



(IV)

The conclusions we draw from these data are that barbaloin contains an aloe-emodinanthrone nucleus, which, unlike the latter, cannot be converted to an enol-derivative.

A substance of formula II would be expected to give rise to an octa-acetate or an octamethyl ether unless an hydroxyl is too sterically hindered to react. In that case the heptamethyl ether should still contain a hydroxyl group. An examination of the infra-red spectrum of the heptamethyl ether failed to reveal any such group. Seven of the nine oxygens are clearly in hydroxyl groups, one in a carbonyl group, so the other is presumably in an ether group (e.g. IV). Formulae containing incompletely aromatic rings with one carbon in the quaternary state can also be suggested. However, they would necessarily be capable of ready aromatization without loss of carbon or migrations involving an aromatic ring, since tetrabromobarbaloin contains a tetrabromoaloe-emodin nucleus (Cahn and Simonsen 1932). Work is being continued, particularly with the halogenobarbaloins.

III. Experimental

(*a*) *Barbaloin.*—This substance was purified by crystallization from aqueous ethanol, m.p. 146–147 °C. Paper chromatography in butanol-acetic acid-water (4 : 1 : 5) or in *m*-cresol-acetic acid-water (25 : 1 : 24) gave only one spot (ferric chloride). Absorption spectra: These were carried out in ethanol. Aloe-emodinanthranol (m.p. 198–199 °C): $\lambda_{max.}$ 258 mμ, log ε 4·07; $\lambda_{max.}$ 290 mμ, log ε 4·13; $\lambda_{max.}$ 355 mμ, log ε 4·06. Aloe-emodinanthranol tetra-acetate (m.p. 195–196 °C): $\lambda_{max.}$ 255 mμ, log ε 4·49; $\lambda_{max.}$ 354 mμ, log ε 3·71; $\lambda_{max.}$ 393 mμ, log ε 3·77.

Heptamethylbarbaloin (m.p. 186–187 °C) after chromatography on alumina and crystallization from ethanol, Cahn and Simonsen (1932) give m.p. 177–179 °C): $\lambda_{max.}$ 280 mμ, log ε 3·93; $\lambda_{max.}$ 320 mμ, log ε 4·04; $\lambda_{max.}$ 372 mμ, log ε 3·87.

Hepta-acetylbarbaloin (see below): $\lambda_{max.}$ 280 mμ, log ε 3·93; $\lambda_{max.}$ 320 mμ, log ε 4·04.

2,2′-Dihydroxybenzophenone (Richter 1883): $\lambda_{max.}$ 260 mμ, log ε 4·07; $\lambda_{max.}$ 336 mμ, log ε 3·76.

2,2′-Diacetoxybenzophenone: $\lambda_{max.}$ 252 mμ, log ε 4·09; $\lambda_{max.}$ 335 mμ, log ε 2·13.

2,2′-Dimethoxybenzophenone: $\lambda_{max.}$ 260 mμ, log ε 3·99; $\lambda_{max.}$ 317 mμ, log ε 3·71.

(*b*) *Hepta-acetylbarbaloin.*—The acetylation was carried out according to Leger (1916). The faintly yellow amorphous product was chromatographed several times in benzene solution on neutral alumina, the first fraction (about 25%) being collected. It could not be crystallized but was precipitated from benzene solution with light petroleum (b.p. 40–70 °C) as a white amorphous solid, m.p. 95–104 °C. This behaviour is in general agreement with that described by Leger (1916). Its formulation as hepta-acetylbarbaloin depends on an acetyl determination (Found: $COCH_3$, 41·6%. Calc. for $C_{21}H_{17}O_2(OCOCH_3)_7$: $COCH_3$, 42·1%).

IV. Acknowledgments

We are indebted to the Rockefeller Foundation (New York) and the University Research Fund for financial assistance.

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STUDIES IN RELATION TO BIOSYNTHESIS

V. THE STRUCTURES OF SOME NATURAL QUINONES

By A. J. Birch* and F. W. Donovan*

[*Manuscript received April* 15, 1955]

Summary

The synthesis of 2,5,7-trimethoxynaphthoquinone (XI) is described. This substance is identical with flaviolin trimethyl ether. Biogenetic relationships of several quinones are discussed.

I. Introduction

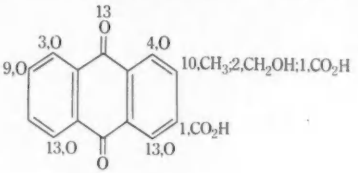
In Part I of this series (Birch and Donovan 1953*a*), the hypothesis was put forward that many natural products are derived by the head-to-tail linkage of acetic acid units, the positions of oxygenated substituents marking the positions of the units. The compounds considered were chiefly phenolic because in such cases reductive removal of the phenolic hydroxyl groups was thought to be unlikely once the aromatic rings had been formed. It is evident that in an incompletely known structure, if some evidence is available from the positions of substituents that it is derived from acetic acid units, then the remaining elements of structure can be defined with a high degree of probability. Such a use of the hypothesis is reminiscent of the well-known use of the isoprene rule. In the case of eleutherinol it has already been possible to correct an erroneous formula (Birch and Donovan 1953*b*). The new formula has since been confirmed (Schmid 1954).

As already pointed out (Birch and Donovan 1953*a*) a number of anthraquinone derivatives can be fitted into the acetate hypothesis. This applies particularly to quinones from moulds (I), and about half the quinones found in higher plants (II). The following frequency diagrams show numerically the occurrences of substituents in the various positions of the ring systems, to be compared with the theoretical distribution (IV). The data were taken from a comprehensive review (Hoffmann-Ostenhof 1950), and the power of the method is shown by the detection of two erroneous formulae in the review ; these are the only definitely assigned formulae omitted in constructing the frequency diagram. They are chrysaron, wrongly formulated as 1,2,7-trihydroxy-6-methylanthraquinone, and rhabarberon, formulated as 1,4,7-trihydroxy-6-methylanthraquinone, which is in fact identical with emodin (4,5,7-trihydroxy-2-methylanthraquinone).

Several points emerge which are not immediately obvious from the forumlae. The additional oxygens at positions 1–(4,OH) and 8–(2,OH) in I are found only

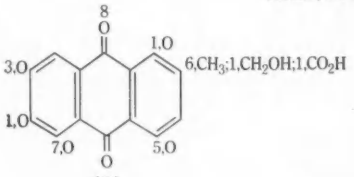
* Department of Organic Chemistry, University of Sydney.

in the presence of the corresponding *para*-hydroxyl groups at the 4- and 5-positions. The extra carbon atom in the 2-position of III (2, CH_3; 2, CO_2H)



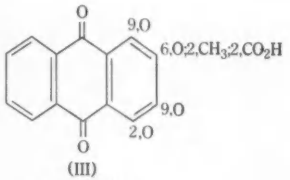
(I)

Moulds, including 2 lichens



(II)

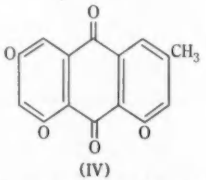
acetate



(III)

non-acetate

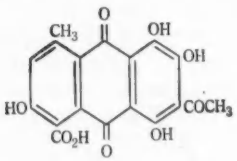
Higher Plants



(IV)

Theoretical; acetate hypothesis

is found only when there are oxygens at the 1- and 3-positions and may well be introduced subsequent to formation of the main skeleton (cf. Birch, Elliott,



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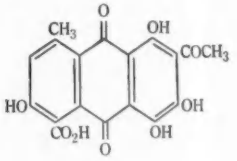

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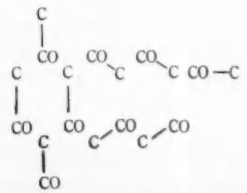


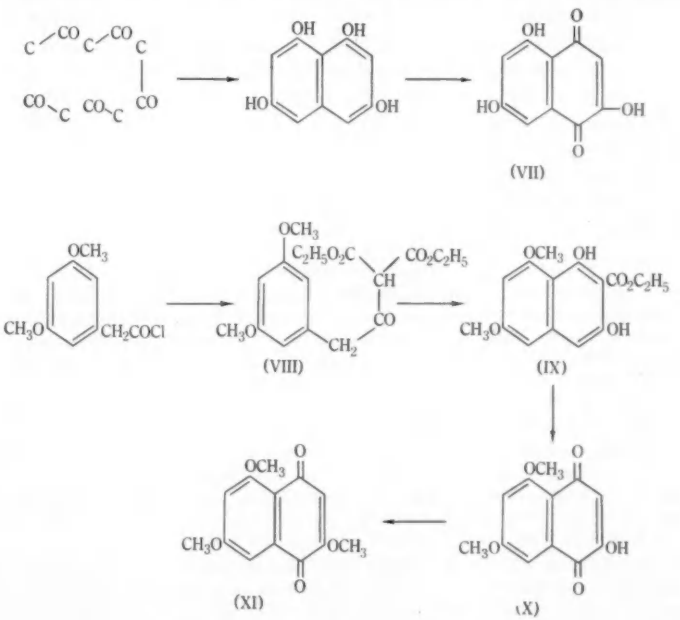
and Penfold 1954). The extra carboxyl group in the 3-position of I is explicable on the acetate hypothesis.

Removal and introduction of oxygen has already been briefly dealt with (Birch and Donovan 1953*a*) and will be considered in more detail in a future paper.

A more complicated case, where the acetate hypothesis can be used to distinguish between alternative formulae in this field, is that of kermesic acid. From purely chemical evidence this has either formula V or VI, the latter being the more probable on the basis of colour reactions (Dimroth and Fick 1916). The acetate hypothesis unequivocally favours the latter also. One hydroxyl group must be introduced by subsequent *para*-oxidation, as well as the quinone oxygen (cf. Birch and Donovan 1953*a*).

II. The Structure of Flaviolin

Owing to the smaller numbers of compounds and greater complexity of substituents, it is not possible to draw up similar numerical schemes for naphthoquinone derivatives. It appears likely that many of these are formed by other biosynthetic routes. However, flaviolin (Astill and Roberts 1953) is a 5,7-*x*-



trihydroxy-1,4-naphthoquinone, where *x* is either 2 or 3. Three of the oxygens are in positions consistent with its formation from acetate units; a fourth quinone oxygen could be rationally introduced by oxidation in the formation of a *p*-quinone. The fifth (*x*-) oxygen should be in the 2-position of the quinone ring if the following biosynthetic scheme is correct. Flaviolin should therefore be VII. The trimethyl ether (XI) was synthesized as shown below and was

found to have the properties characteristic of flaviolin trimethyl ether (Astill and Roberts 1953). (Synthetic: m.p. 186–187 °C from benzene-light petroleum, $\lambda_{max.}$ 260, 296, 416 mμ, log $\varepsilon_{max.}$ 4·20, 4·05, 3·52; natural: m.p. 186–187 °C from ethanol or 191 °C from aqueous methanol, $\lambda_{max.}$ 258, 296, 417 mμ, log $\varepsilon_{max.}$ 4·31, 4·13, 3·50; these values were taken from a small-scale curve.)

Since a preliminary note was published giving the above conclusions (Birch and Donovan 1954) Davies, King, and Roberts (1954) have also synthesized flaviolin trimethyl ether (XI) by a different route and have shown the identity of natural and synthetic material.

Structures can also be assigned to the naphthoquinones, fusarubin and javanicin, on the basis of the acetate hypothesis (Birch and Donovan 1954).

III. Synthesis of Flaviolin Trimethyl Ether

3,5-Dimethoxyphenylacetyl chloride was condensed with the diethyl ethoxymagnesiomalonate to form ethyl 2-carbethoxy-3-keto-4-(3′,5′-dimethoxyphenyl)butyrate (VIII) which readily cyclized with polyphosphoric acid (Birch, Jaeger, and Robinson 1945) to form ethyl 1,3-dihydroxy-6,8-dimethoxynaphthalene-2-carboxylate (IX). Hydrolysis of this ester with cold sodium hydroxide solution in the presence of air resulted in the expected decarboxylation and oxidation to give what is evidently the hydroxydimethoxynaphthoquinone (X). This was available only in small amount, and was difficult to purify, so was converted immediately by reaction with methanolic hydrogen chloride to 2,5,7-trimethoxynaphthoquinone (XI) (flaviolin trimethyl ether). This method of etherification was found to be superior to the use of methyl sulphate and alkali (Astill and Roberts 1953).

IV. Experimental

(*a*) *Ethyl 2-Carbethoxy-3-keto-4-(3′,5′-dimethoxyphenyl)butyrate.*—A solution of diethyl ethoxymagnesiomalonate was prepared from magnesium (1·0 g), ethanol (4 c.c.), and diethyl malonate (6·6 g) in dry ether (25 c.c.) in the presence of 3 drops of carbon tetrachloride (Walker and Hauser 1946). The ether and excess ethanol were removed by distillation with benzene. 3,5-Dimethoxyphenylacetyl chloride from 3,5-dimethoxyphenylacetic acid (Birch and Donovan 1953*b*) (2·5 g) and phosphorus trichloride (0·65 g) in benzene was slowly added to the above solution and the mixture refluxed for 1 hr.

After cooling and acidification, the benzene layer was separated, the solvent removed, and excess diethyl malonate taken off at 110 °C/1 mm. The residue crystallized (3·65 g) and was used directly for the next step. A sample was crystallized for analysis, first from aqueous ethanol, then twice from light petroleum (b.p. 60–80 °C) to form white needles, m.p. 66–67 °C (Found: C, 60·4; H, 6·4%. Calc. for $C_{17}H_{22}O_7$: C, 60·3; H, 6·6%).

(*b*) *Ethyl 1,3-Dihydroxy-6,8-dimethoxy-2-naphthoate.*—A mixture of diethyl 3,5-dimethoxyphenylacetylmalonate (above) and a solution of phosphorus pentoxide (5·0 g) in syrupy phosphoric acid (5·0 c.c.) was kept at 100 °C for 5 min with stirring. It was cooled, diluted with water (80 c.c.), and the gummy solid taken up in ether. The extract was washed with sodium bicarbonate solution, dried, and the solvent removed to leave a yellow crystalline solid (1·2 g). For analysis it was crystallized from ether-light petroleum (b.p. 40–70 °C) and then from ethanol as yellow prisms, m.p. 122–123 °C (Found: C, 61·7; H, 5·5%. Calc. for $C_{13}H_{16}O_6$: C, 61·6; H, 5·5%).

(*c*) *2,5,7-Trimethoxy-1,4-naphthoquinone.*—A solution of ethyl 1,3-dihydroxy-6,8-dimethoxy-2-naphthoate (153 mg) in aqueous potassium hydroxide (5 c.c.; 5%) rapidly darkened to a deep reddish brown colour. The solution was left for 4 days in an unstoppered flask. On acidification

a red gum (150 mg) separated which solidified on scratching, m.p. (crude) about 75 °C. It was found to be difficult to purify and was directly converted to the trimethyl ether. The crude product (300 mg) was refluxed with methanolic hydrogen chloride (10 c.c.; 4%) for 1·5 hr, evaporated to dryness under reduced pressure, and the residue taken up in hot benzene (20 c.c.). The solution was chromatographed in benzene on acid-washed alumina to give a yellow band eluted with benzene-ether (1 : 1). The eluate was a yellow crystalline solid, m.p. *c.* 170 °C which was crystallized from benzene-light petroleum (b.p. 40–60 °C) as deep yellow prisms, m.p. 186–187 °C (Found: C, 62·9; H, 4·95%. Calc. for $C_{13}H_{12}O_5$: C, 62·9; H, 4·9%). The ultraviolet absorption spectrum was determined in 95% ethanol and is described above.

V. Acknowledgments

The authors are indebted to the Rockefeller Foundation (New York) for financial assistance.

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STUDIES IN RELATION TO BIOSYNTHESIS

VI. RHEOSMIN

By L. Bauer,* A. J. Birch,* and A. J. Ryan*

[*Manuscript received April* 15, 1955]

Summary

Benzalpiperitone (I) has been dehydrogenated to 3-hydroxy-4-*iso*propylstilbene (II), which on ozonolysis gave rise to 3-hydroxy-4-*iso*propylbenzaldehyde (IV), which is unlikely to be identical with rheosmin. This substance appears on the basis of its properties and possible biosynthesis to be 1-(*p*-hydroxyphenyl)butan-3-one (V).

I. Introduction

Gilson (1903) hydrolysed the substance tetrarin from Chinese rhubarb, obtaining a compound, rheosmin, $C_{10}H_{12}O_2$, m.p. 79·5 °C, which showed the properties of a phenol and a carbonyl compound, giving rise to a crystalline bisulphite derivative and an oxime of unspecified properties. It showed reducing properties towards ammoniacal silver, and gave a Schiff's test, so Gilson thought it to be an aldehyde. Freudenberg (1920) suggested that rheosmin is probably an hydroxycuminaldehyde. Recently, "macropone" was shown to be 2-hydroxycuminaldehyde (2-hydroxy-4-*iso*propylbenzaldehyde) (Birch and Elliott 1953) which is an oil solidifying well below zero and cannot be identical with rheosmin. If Freudenberg's suggestion is correct and the substance is isoprenoid as suggested by the C_{10}-formula, the most likely remaining formulation would be 3-hydroxy-4-*iso*propylbenzaldehyde (IV) and this compound has therefore been synthesized. It has not been obtained crystalline even after 6 months in a refrigerator. Gilson (1903) implies that there was no difficulty in crystallizing rheosmin, and it is therefore unlikely to be identical with IV. No details of the isolation of tetrarin were given by Gilson, and we have been unable so far to obtain either tetrarin or rheosmin from East Indian rhubarb.

II. Synthesis of 3-Hydroxy-4-*iso*propylbenzaldehyde

(±)-Benzalpiperitone has the formula I (Earl and Smith (1921), Earl (1922), Earl and Read (1926)) and its preparation was readily repeated. It was first obtained in an α-form (prisms, m.p. 59–61 °C) and a β-form (rhombs, m.p. 63–64 °C), but later only in a γ-form (needles, m.p. 69–70 °C). In our first preparation we obtained a mixture of the α- and predominantly the β-form, in the second only the γ-form. The ultraviolet spectra of the β- and γ-forms were found to be identical ($\lambda_{max.}$ 237 mμ, log ε 3·91 ; $\lambda_{max.}$ 322 mμ, log ε 4·53)

* Department of Organic Chemistry, University of Sydney.

thus excluding the possibility that they are *cis-trans*-isomers and confirming that the difference is merely one of crystalline form.

Attempts to oxidize benzalpiperitone with ferric chloride in acetic acid gave only intractable tars, but dehydrogenation of the *cyclo*hexenone ring took place with palladium-charcoal. The product was a mixture of the stilbene II and the dibenzyl III. Distillation and crystallization afforded both substances in a state of purity although in rather low yield. They readily formed mixed crystals. Their ultraviolet spectra (Fig. 1) showed expected differences. The

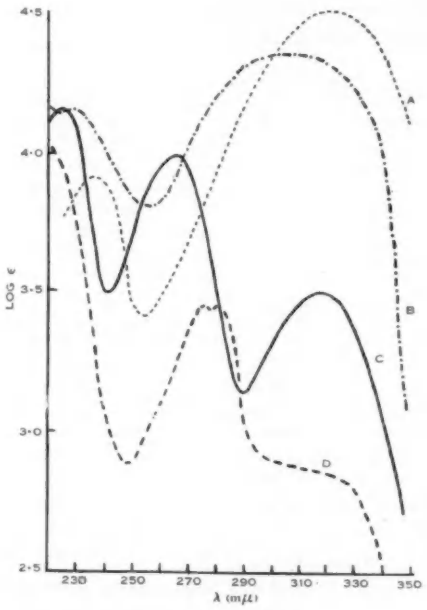


Fig. 1.—Ultraviolet absorption spectra.
A, Benzalpiperitone (I).
B, 3-Hydroxy-4-*iso*propylstilbene (II).
C, 3-Hydroxy-4-*iso*propylbenzaldehyde (IV).
D, 3-Hydroxy-4-*iso*propyldibenzyl (III).

stilbene II was ozonized as its *p*-nitrobenzoate and methanolysis of the product gave 3-hydroxy-4-*iso*propylbenzaldehyde. It was later found that the procedure of Bonner and Collins (1953) for the ozonolysis of stilbene itself, using ethanolic sulphuric acid as the solvent gave IV in good yield directly from II. The part played by the solvent is not clear, possibly acetals are formed, but the general procedure seems worthy of further investigation in degradative work.

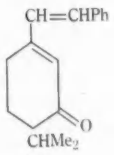
The present work constitutes further proof of the formula I assigned by Earl and Smith (1921), Earl (1922), and Earl and Read (1926) to benzalpiperitone.

III. 1-(*p*-Hydroxyphenyl)butan-3-one

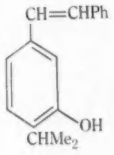
If rheosmin is not an isoprenoid phenol then general biosynthetic considerations suggest that it may be a derivative of the C_6–C_3 series, and the most probable structure on this basis is 1-(*p*-hydroxyphenyl)butan-3-one (V). It would thus be closely related to zingerone which possesses an extra methoxyl group in the *meta*-position.

Although V is a ketone, and not an aldehyde, as proposed for rheosmin by Gilson (1903), the resemblance is otherwise close:

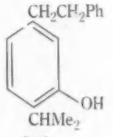
Rheosmin, m.p. 79·5 °C, forms rhombic needles, is soluble in ethanol and ether, is less soluble in benzene and light petroleum, forms an oxime (no m.p. given) and a crystalline bisulphite derivative.



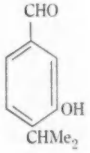
(I)



(II)



(III)



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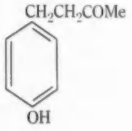

(V)

1-(*p*-Hydroxyphenyl)butan-3-one, m.p. 81 °C, forms colourless needles, has similar solubilities to those above, gives an oxime, m.p. 97–98 °C and a crystalline bisulphite derivative.

It is noteworthy that zingerone also reduces ammoniacal silver nitrate (Nomura 1917).

The synthetic compound was found to give a positive Schiff's test, and a silver mirror with ammoniacal silver nitrate after warming to 100 °C for 5 min. Gilson's evidence for the presence of an aldehyde, rather than a ketone grouping, would therefore not apply in this case. We accordingly believe rheosmin to be identical with V.

IV. Experimental

Melting points are uncorrected; ultraviolet spectra were carried out in ethanol distilled from sodium hydroxide and zinc dust.

(*a*) *3-Hydroxy-4-isopropylstilbene.*—Benzalpiperitone (10·3 g) was refluxed for 10 hr in diphenyl ether (70 c.c.) and trimethylene glycol (30 c.c.) in the presence of palladium-charcoal catalyst (10 g, 5%; Organic Syntheses 1946). The solution was cooled to 60 °C, the catalyst removed by filtration and washed with ethyl acetate. The organic layer was extracted with three successive portions (30 c.c.) of a solution of potassium hydroxide (35 g) in water (25 c.c.) diluted to 100 c.c. with methanol (Claisen's alkali). The extract was washed with benzene

(30 c.c.) and the benzene, together with the original organic layer, again extracted with Claisen's alkali. The combined alkaline solution was extracted with light petroleum, diluted with water, acidified, and the phenols extracted with ether-benzene. Distillation gave fraction *A* (3·9 g), b.p. 160–170 °C/1 mm and fraction *B* (1·3 g), b.p. 170–180 °C/1 mm. Fraction *A* was redistilled, b.p. 163 °C/1 mm, and crystallized from light petroleum (b.p. 40–60 °C) at —10 °C to give *3-hydroxy-4-isopropyldibenzyl*, m.p. 33 °C; $\lambda_{max.}$ 276 mμ, log ε 3·46; $\lambda_{max.}$ 282 mμ, log ε 3·46 (Found: C, 85·0; H, 8·2%. Calc. for $C_{17}H_{20}O$: C, 85·0; H, 8·3%). The ultraviolet absorption curve (Fig. 1) showed that not more than about 3% of II was present. Fraction *B* was crystallized from light petroleum (b.p. 40–60 °C) to give colourless needles of *3-hydroxy-4-isopropylstilbene*, m.p. 97–98 °C; $\lambda_{max.}$ 228 mμ, log ε 4·16; $\lambda_{max.}$ 310 mμ, log ε 4·36 (Found: C, 85·4; H, 7·5%. Calc. for $C_{17}H_{18}O$: C, 85·7; H, 7·6%).

The stilbene (500 mg), pyridine (10 c.c.), and *p*-nitrobenzoyl chloride (800 mg) were heated to 100 °C for 1 hr and poured into water. After trituration with sodium hydrogen carbonate solution the *p-nitrobenzoate* was obtained as yellow rhombs (0·62 g), m.p. 85–86 °C (Found: C, 74·5; H, 5·6%. Calc. for $C_{24}H_{21}O_4N$: C, 74·4; H, 5·4%.

(*b*) *3-Hydroxy-4-isopropylbenzaldehyde.*—(i) The above *p*-nitrobenzoate (600 mg) in ethyl acetate (25 c.c.) was ozonized at —10 °C for ½ hr, excess ozone removed with nitrogen and aqueous ferrous sulphate added. After 1 hr the organic layer was separated, again shaken with ferrous sulphate solution, washed with $NaHCO_3$ solution and saturated brine, and then evaporated. The resulting gum could not be crystallized, but gave rise to *3-p-nitrobenzoyloxy-4-isopropylbenzaldehyde-2,4-dinitrophenylhydrazone* as brick red rhombs from acetic acid, m.p. 292–293 °C (Found: C, 55·7; H, 3·95; N, 13·7%. Calc. for $C_{22}H_{19}O_8N_5$: C, 56·0; H, 3·9; N, 14·2%). The gum was dissolved for ½ hr in alcoholic alkali (25 c.c.) on the steam-bath. Worked up in the usual way the product distilled over a wide range, 100–160 °C/1 mm but gave rise to the derivatives of 3-hydroxy-4-*iso*propylbenzaldehyde: *2,4-dinitrophenylhydrazone*, scarlet plates from benzene m.p. 244 °C (Found: C, 55·3; H, 4·8%. Calc. for $C_{16}H_{16}O_5N_4$: C, 55·8; H, 4·7%) and *semicarbazone*, m.p. 175–176 °C (Found: C, 59·7; N, 6·7%. Calc. for $C_{11}H_{13}O_2N_3$: C, 59·7; H, 6·8%).

(ii) A solution of the stilbene (240 mg) in ethanol (25 c.c.), containing conc. sulphuric acid (0·5 c.c.), was rapidly ozonized at 0 °C for 25 min. The solution was worked up as above, extracting with ethyl acetate. The first fraction from the distillation consisted of benzaldehyde, identified as its 2,4-dinitrophenylhydrazone (110 mg), m.p. 236–237 °C, undepressed by an authentic specimen. The second fraction was redistilled to give *3-hydroxy-4-isopropylbenzaldehyde*, b.p. 135 °C/1 mm, $n_D^{14°}$ 1·5575; $\lambda_{max.}$ 225 mμ, log ε 4·16; $\lambda_{max.}$ 265 mμ, log ε 3·99; $\lambda_{max.}$ 318 mμ, log ε 3·51 (Found: C, 73·1; H, 7·5%. Calc. for $C_{10}H_{12}O_2$: C, 73·1; H, 7·3%. In another experiment the stilbene (350 mg) gave the aldehyde (200 mg) in a yield of 87%. It was purified through the crystalline sodium bisulphite derivative and by extraction into dilute NaOH solution, but could not be crystallized at 0 °C for 6 months, or by precipitation from alkaline solution with CO_2 as described by Gilson (1903).

(*c*) *1-(p-Hydroxyphenyl)butan-3-one.*—Prepared according to Mannich and Merz (1927) and purified through the crystalline bisulphite compound 1-(*p*-hydroxyphenyl)butan-3-one formed colourless needles, m.p. 81 °C (lit. 83·5–84·5 °C). The *2,4-dinitrophenylhydrazone* formed orange plates, m.p. 145–146 °C (Found: C, 55·7; H, 4·9%. Calc. for $C_{16}H_{16}O_5N_4$: C, 55·8; H, 4·7%); the *semicarbazone* formed colourless needles, m.p. 152–153 °C (Found: C, 59·6; H, 6·7%. Calc. for $C_{11}H_{15}O_2N_3$: C, 59·7; H, 6·8%).

V. Acknowledgments

The authors are indebted to the Rockefeller Foundation (New York) and Dr. A. Ungar (Andrews Laboratories) for financial assistance.

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STUDIES IN RELATION TO BIOSYNTHESIS

VII. 2-HYDROXY-6-METHYLBENZOIC ACID IN PENICILLIUM GRISEOFULVUM DIERCKX

By A. J. Birch,* R. A. Massy-Westropp,* and C. J. Moye*

[*Manuscript received May* 9, 1955]

Summary

The general problem of the biosynthesis of depsides and depsidones is considered. Feeding experiments using sodium acetate isotopically labelled in the carboxyl group have demonstrated that the mould *Penicillium griseofulvum* Dierckx (Raistrick's strain P68) elaborates 2-hydroxy-6-methylbenzoic acid (VII) by the head-to-tail linkage of acetic acid units in accord with the hypothesis of Birch and Donovan (1953). This demonstration constitutes the first definite support for the hypothesis based on biochemical experiments.

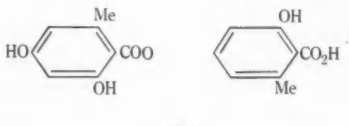
I. Introduction

In Part I (Birch and Donovan 1953) it was shown by structural analysis that the biosynthesis of many phenolic compounds may occur by the head-to-tail linkage of acetic acid units.† The depsides found in many lichens illustrate an important branch of the scheme, and we have now analysed the frequency of occurrence of various substituents attached to the aromatic units of these substances. The data are taken from a review by Nolan (1946), all the authenticated formulae there given being included. Typical substances of the depside and depsidone types are respectively lecanoric acid (I) and physodic acid (II). Formula III shows the numerical occurrence of substituents in units of the former type, which are joined merely by esterification. Formula IV comprises the depsidones which contain an ether link joining the 2-position of one unit with the 5-position of the other. The two units are shown separately to avoid confusion due to the extra carbon-oxygen link. No account need be taken for present purposes of the attachment of ester or methyl groups to the oxygens, since the formation of such groups is presumably secondary and due to processes not directly concerned with the elaboration of the main skeleton. We consider that extra substituents attached to C–3 are introduced by secondary processes (cf. Birch, Elliott, and Penfold 1954; Birch and Elliott 1956). Unlike substituents in the 1-, 2-, 4-, and 6-positions which involve exclusively either C–O or C—C links according to the position, these may involve either a C—O or a C—C link and they are less frequent. All the side-chains encountered contain an odd number of carbon atoms, in accord with their origin from normal fatty

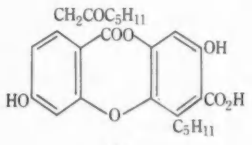
* Department of Organic Chemistry, University of Sydney.

† This hypothesis was first announced in lectures at the Universities of Birmingham and Liverpool in March 1952.

acids. With one exception carbonyl groups in the side-chain are in the β-position, presumably marking an extra unreduced acetate unit. The exception is found in lobaric acid, a depsidone with COC_4H_9 in one nucleus, and C_5H_{11} in the other. The carbonyl next to the aromatic ring could conceivably be introduced by oxidation, especially in view of the probability that the depsidone structure is produced by an oxidative condensation, and the fact that depsidones are generally at a higher oxidation level than the depsides. It is notable, although not at present explicable, that all the depsides which carry Me, CHO, or CO_2H at C–3 also have only a C_1 side-chain at C–6, and that C_1 and C_5 side-chains are more frequent than C_3 and C_7.



(I)



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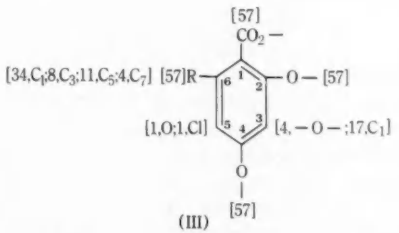


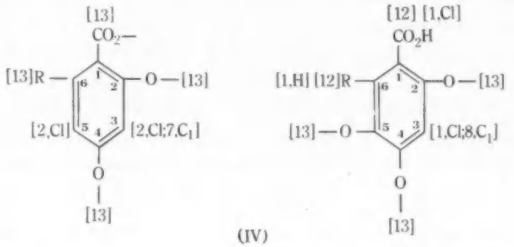
(III)

1-Position: 26,CO_2H; 31,CO_2–. 2-Position: 55,OH; 2,OMe. 3-Position: 1,OH; 3,–OCO–; 9,Me; 6,CHO; 2,CO_2H. 4-Position: 11,OH; 20,OMe; 26,–OCO–. 5-Position: 1,Cl; 1,OH. 6-Position: 33,Me; 1,CH_2OH; 8,C_3H_7; 10,C_5H_{11}; 1,C_7H_{15}; 3,$CH_2COC_5H_{11}$; 1,$CH_2COC_3H_7$.

Whether or not the acetate hypothesis is accepted as the explanation, it seems clear from III and IV that the structures of the units found in depsides and depsidones have a common factor which can be expressed as V. According to the hypothesis this is generated structurally by condensation of the units shown in VI, where R may be Me, or any odd-numbered chain itself generated biologically from acetic acid in the manner already demonstrated for normal fatty acids.

The only obvious method to test the hypothesis is by the use of isotopically labelled acetic acid in feeding experiments. Lichens would be difficult to use for experimental reasons, but the compounds they form appear to be mould metabolic products, since lichens are symbionts of moulds and algae, and a number of these compounds with structures similar to the units of depsides and depsidones have been isolated from moulds by Raistrick and his co-workers (e.g. Raistrick 1950*a*, 1950*b*). The most suitable mould for the present purpose

appeared to be *Penicillium griseofulvum* Dierckx (Raistrick's strain P68) which was kindly supplied by Dr. P. W. Brian. It produces considerable quantities of 2-hydroxy-6-methylbenzoic acid (VII) when grown on a glucose medium. The mould would have no difficulty in producing acetic acid by known biochemical routes from such a medium. This substance (VII) has lost the oxygen



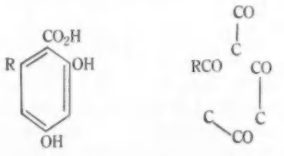
(IV)

1-Position : 13,–CO_2–.
2-Position : 13,–O–.
3-Position : 2,Cl ; 7,CHO.
4-Position : 10,–OH ; 3,–OMe.
5-Position : 2,Cl.
6-Position : 9,Me ; 3,$CH_2COC_5H_{11}$1,COC_4H_9.

1-Position : 12,CO_2H ; 1,Cl.
2-Position : 11,–OH ; 2,OMe.
3-Position : 1,Cl ; 3,Me ; 3,CH_2OH ; 2CH_2OR'.
4-Position : 13,–OCO–.
5-Position : 13,–O–.
6-Position : 1,H ; 3,Me ; 5,CHO ; 2,C_5H_{11} ; 2,$CH_2COC_5H_{11}$.

from the 4-position, but such a loss is compatible with biosynthesis from acetic acid (Birch and Donovan 1953 ; Birch and Elliott 1956). The distribution of ^{14}C to be expected from direct incorporation of $CH_3{}^{14}CO_2H$ is shown in VII (^{14}C marked by *).

The degradations shown below seem to be compatible only with VII and therefore indicate direct biosynthesis from acetic acid. The carbon dioxide from combustion of the whole molecule should show half the activity of that



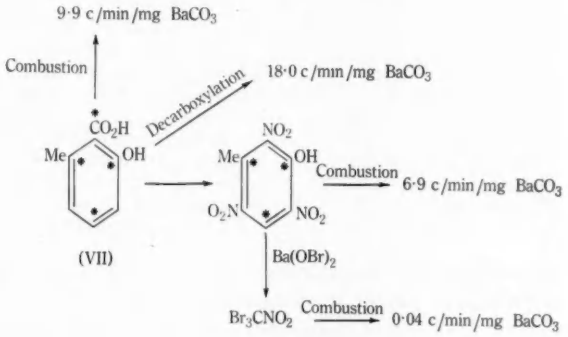
(V) (VI)

from the carboxyl and the activity of carbon dioxide from combustion of the trinitro-*m*-cresol should be 0·248 times that from the carboxyl, that is, 7·7 c/min/mg $BaCO_3$. The bromopicrin (Birch and Moye 1956) should be quite inactive since it arises from methyl in the acetic acid.

The departures from the theoretical of the values determined do not appear to be significant. The slightly high figure for the total combustion might be due to incomplete combustion, which would give a product containing a slightly high proportion of carbon dioxide from the carboxyl group. The 3-methyl-2,4,6-

trinitrophenol had m.p. 95–98 °C (lit. m.p. 109·5 °C) and could not be purified further because of the small amount available. It may contain a little 3-carboxy-2,4,6-trinitrophenol, found in larger-scale experiments with inactive material, which would account for the slightly low value. The figure 0·04 count/min/mg for the bromopicrin product does not differ significantly from zero. Other degradations are in progress.

The circumstantial evidence in favour of the general hypothesis is so strong for a number of other classes of compound (Birch and Donovan 1953) that definite biochemical proof in a few selected cases, such as that above, will in our opinion establish its validity over a wide field. We wish to emphasize again (cf. Birch and Donovan 1953) that there are clearly other methods of biosynthesis of natural phenolic compounds, and some possible routes are under investigation.



The acetate theory is at present a purely structural one; there are, for example, at least three quite distinct sequences which would lead to the production of VII from acetic acid, and we are engaged in the examination by tracer methods of possible intermediate stages.

II. Experimental

(*a*) *Labelled 2-Hydroxy-6-methylbenzoic Acid.—Penicillium griseofulvum* (Raistrick's strain P68) was grown under the conditions described by Anslow and Raistrick (1931). Preliminary experiments showed that it was important to keep the temperature constant at 26·5 °C to obtain good yields. Two flasks, each containing 350 c.c. of medium, were grown for 10 days, when a solution containing 0·033 m.c. of carboxyl labelled sodium acetate was added to each flask. Growth was continued until the 15th day, when the metabolite was isolated according to Anslow and Raistrick (1931). 2-Hydroxy-6-methylbenzoic acid (0·6 g), m.p. 167 °C, resulted after recrystallization.

(*b*) *Degradation of 2-Hydroxy-6-methylbenzoic Acid.*—The carbon dioxide, obtained by the methods outlined below, was converted to barium carbonate by passage into a solution of barium hydroxide octahydrate (2%) containing potassium nitrate (3%) to assist granulation of the fine precipitate. The precipitate (about 20–25 mg) was filtered on a tared filter in a stainless steel tapered funnel and separate filter mount, which fitted closely the base of the funnel and had a hollow stem to which suction was applied. After thorough washing the paper and precipitate were dried and weighed and the activity examined. The apparatus was arranged to exclude atmospheric carbon dioxide.

The apparatus used for determination of radioactivity consisted of an SC3/100 Austronic scaling unit in conjunction with an EHM 2S Geiger tube, the sample being placed in a lead castle (Oddie and Mibus 1949). Correction factors for self-absorption only were applied, since all other factors were kept constant as far as possible. To obtain the intrinsic activity the figures below must be multiplied by a factor of 14·2.

(i) *Combustion.* This was carried out in a slightly simplified version of a usual micro-combustion furnace.

(ii) *Decarboxylation.* Rapid evolution of carbon dioxide occurred on heating to 180 °C in solution in pure quinoline in the presence of a trace of copper powder. The carbon dioxide was carried into the barium hydroxide solution in a current of pure oxygen.

(iii) *Preparation of 3-methyl-2,4,6-trinitrophenol.* Although direct nitration of the acid yields 3-methyl-2,4,6-trinitrophenol, better yields were obtained by preliminary decarboxylation to *m*-cresol. The best yield was obtained by dissolving *m*-cresol (200 mg) in sulphuric acid (1·0 c.c.), addition of nitric acid (0·4 c.c., *d* 1·4) in sulphuric acid (0·8 c.c.) in the cold, followed by nitric acid (0·65 c.c., *d* 1·4) and heating on the steam-bath for 90 min. The mixture was cooled in the refrigerator and the product (410 mg) removed by filtration and washed with water. Dilution with water and ether extraction gave very little more material which was less pure.

(iv) *Bromopicrin Degradation.* Radioactive 3-methyl-2,4,6-trinitrophenol (60 mg) was reacted with barium hydroxide and bromine (Birch and Moye 1956) and the steam-distilled bromopicrin (130 mg) separated by centrifuging and washed three times with distilled water, then undergoing combustion in the usual apparatus and the barium carbonate estimated as above.

The results presented in Table 1 were obtained.

TABLE 1

Treatment	$BaCO_3$ (mg)	Corrected Count/ min/mg	Average Counts/ min/mg
Decarboxylation (C–1′)	21·1	17·89	18·0±0·12*
	25·8	18·46	
	21·1	17·65	
Combustion of:	18·16	9·96	9·9±0·09*
Acid			
(C–1+C–1′+C–2+C–3 ..	20·25	9·60	
+C–4+C–5+C–6+C–6′) ..	22·00	10·20	
Trinitro-*m*-cresol	12·53	6·91	6·9±0·1*
(C–1+C–2+C–3+C–4+C–5			
+C–6+C–6′)			
Brompoicrin	15·46	0·04	0·04
(C–1+C–3+C–5)			

* The errors given are standard deviations of the counts and would not take account of systematic errors (see above). We do not consider that such errors would be greater than a maximum of 1·0 count/min/mg.

III. ACKNOWLEDGMENTS

This work was made possible by the Nuffield Foundation which provided apparatus and a Scholarship (C.J.M.), and the Rockefeller Foundation (New York) which provided a scholarship (R.A.M-W.). We are greatly indebted to Professor H. Raistrick, F.R.S., for a helpful discussion when the work was initiated, to Dr. P. W. Brian (I.C.I., Welwyn) who provided the mould, to Dr.

B. J. Ralph who supplied facilities for the biological work at the N.S.W. University of Technology, to Mr. K. R. Lynn (C.S.I.R.O., Melbourne), and Dr. R. E. B. Makinson who assisted us with the radiotracer work.

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STUDIES IN THE CHEMISTRY OF PHENOTHIAZINE

I. SUBSTITUTED *o*-AMINOBENZENETHIOLS

By K. J. FARRINGTON* and W. K. WARBURTON*

[*Manuscript received July 8, 1955*]

Summary

The preparation of some chloro-substituted *o*-aminobenzenethiols, and their conversion to phenothiazines, are described. The scope and limitations of some methods for preparing the former are discussed.

I. INTRODUCTION

Biological work in progress at this laboratory and elsewhere has required the preparation of various substituted phenothiazines. Two of these, 2,7-dichlorophenothiazine (I) and 3,7-dichlorophenothiazine (II) cannot be made conveniently and unambiguously, except by the Smiles rearrangement of the appropriate diphenyl sulphides. These, in turn, are prepared from the *o*-aminobenzenethiols and *o*-halonitrobenzenes. A review of the methods available for preparing substituted *o*-aminobenzenethiols showed that 2-amino-4-chlorobenzenethiol (III) had been described, but that the synthetic procedure and identity of the compound required reinvestigation, whereas the isomers 2-amino-3-chlorobenzenethiol (IV), 2-amino-5-chlorobenzenethiol (V), and 2-amino-6-chlorobenzenethiol had not been described, although there was a general reference to the metal salts of compounds of this type.

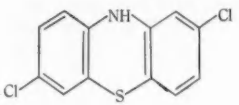
II. PREPARATION OF *o*-AMINOBENZENETHIOLS

It has been reported (Cassella and Co. 1922) that the chloroanilines, like aniline, undergo the Herz reaction with sulphur chloride to give nuclear-chlorinated thiazathiolium chlorides which, on alkaline hydrolysis, give the salts of the chlorinated *o*-aminobenzenethiols. These are isolated and used in condensations as the zinc mercaptides. This reaction has been used with success to prepare salts of 2-amino-5-bromobenzenethiol and 2-amino-5-dimethylaminobenzenethiol (e.g. Stephens and Wibberley 1950), but there is no report subsequent to the original patent of the preparation of a substituted *o*-aminobenzenethiol with a free 5-position. In this laboratory the reaction proceeded well with *p*-chloroaniline to give V, but with *m*-chloroaniline nothing recognizable was obtained on hydrolysis of the small amount of the Herz compound isolated. With *o*-chloroaniline, the only product was 2-amino-3,5-dichlorobenzenethiol, and nuclear substitution could not be avoided, despite many attempts to moderate the reaction. This substitution reaction is mentioned in the original patent.

* Division of Animal Health and Production, C.S.I.R.O., McMaster Laboratory, Sydney.

It is concluded that the Herz reaction is of no value for preparing substituted *o*-aminobenzenethiols with a free 5-position. The Herz reaction has been discussed by Bezzubets (1947).

Other methods examined for the preparation of benzenethiols included reduction of the diphenyl disulphide, hydrolysis of benzothiazole derivatives and chlorination of *o*-acetamidobenzenethiol or of the disulphide obtained from it by oxidation. 2,2′-Diacetamidodiphenyl disulphide was readily prepared, whereas selective *N*-acylation of *o*-aminobenzenethiol was found to be difficult and wasteful. Consequently substitution experiments were confined to the diacetamido disulphide. Although this compound was readily substituted, a complex mixture was formed and neither V nor IV could be detected as their



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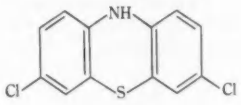

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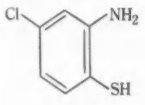

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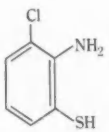

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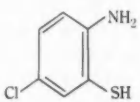

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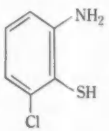

(VI)

acetyl derivatives in the reduced products. The work of Teppema and Sebrell (1927) indicated a route to V, by hydrolysis of 6-chloro-2-mercaptobenzothiazole, but conditions required to open the thiazole ring were so drastic that the halogen atom was removed, presumably by hydrogen sulphide. However, alkaline hydrolysis of 2-(2,4-dichloroanilino)-6-chlorobenzothiazole, which is not readily available, is reported to give V (Lubs and Cole 1935).

The reduction of the appropriate dinitrodiphenyl disulphide furnished III in good yield. Hodgson and Wilson (1925) reported the formation of III in unspecified yield from the direct reaction of 2,5-dichloronitrobenzene and sodium disulphide in water; presumably by formation and reduction of the diphenyl disulphide. However, their compound (m.p. 120 °C) was not analysed. Pollak, Reisz, and Kahane (1928) reported the same compound as a dark yellow oil from reduction of the disulphide with zinc and acetic acid, whereas Lankelma and Knauf (1931), who reduced the disulphide with tin and hydrochloric acid and decomposed the amine hydrochloride with sodium bicarbonate, reported that the free amine melted at 198–201 °C and was readily oxidized by air. It was found in this laboratory that reduction of the disulphide with zinc and acetic acid gave the zinc salt of III in good yield, and from this the amine was obtained, m.p. 119–121 °C (cf. Hodgson and Wilson 1925), which was unaffected

by air after several months' exposure. Reduction of 4,4'-dichloro-2,2'-dinitrophenyl disulphide with sodium sulphide and hydrogen sulphide in ethanol gave only 4-chloro-2-nitrobenzenethiol.

III. Preparation of Phenothiazines

2,7-Dichlorophenothiazine (I) has not been described before, but a compound (m.p. 222 °C) presumed to be 3,7-dichlorophenothiazine (II) was formed in small yield, together with other products, on direct chlorination of phenothiazine (Unger and Hoffman 1896). The Smiles rearrangement, which has recently been reviewed (Massie 1954), when applied to the diphenyl sulphide prepared by condensing III with 2,5-dichloronitrobenzene and acetylating the product, gave **I** in high yield, and V in the same sequence of reactions gave II. On the other hand, Baltzly, Harfenist, and Webb (1946) found that 2-acetamido-4-bromo-4'-nitrodiphenyl sulphide did not rearrange. Attempts to prepare II by fusion of 4,4'-dichlorodiphenylamine failed.

Work is proceeding on the preparation of other *o*-aminobenzenethiols and phenothiazines.

IV. Experimental

Melting points are corrected. Analyses are by Dr. K. W. Zimmermann, C.S.I.R.O. Microanalytical Laboratory.

(*a*) *4,4'-Dichloro-2,2'-dinitrodiphenyl Disulphide.*—A solution of sulphur (4·8 g) and hydrated sodium sulphide (36 g) in ethanol (300 ml) was cautiously added to a refluxing solution of 2,5-dichloronitrobenzene (38·4 g) in ethanol (50 ml). After 3 hr refluxing the mixture was chilled, and the filtered product washed with water to give pale yellow, rectangular plates, m.p. 208–211 °C (decomp.). Yield 27·2 g, 72%. A sample recrystallized from a large volume of ethanol had m.p. 215 °C (decomp.) (Found: C, 38·4; H, 1·85; N, 7·5%. Calc. for $C_{12}H_6O_4N_2S_2Cl_2$: C, 38·2; H, 1·6; N, 7·4%).

(*b*) *4-Chloro-2-nitrobenzenethiol.*—Reduction of (*a*) with sodium sulphide and hydrogen sulphide in boiling ethanol for 24 hr followed by acidification gave a 20% yield of *4-chloro-2-nitrobenzenethiol*, pale yellow, short, thick needles from ethanol, m.p. 146–147 °C, soluble in alkali but not in dilute acid (Found: N, 7·5%. Calc. for $C_6H_4O_2NSCl$: N, 7·4%).

(*c*) *2-Amino-4,4'-dichloro-2'-nitrodiphenyl Sulphide.*—The sodium salt of 2-amino-4-chlorobenzenethiol (2·10 g) (containing a small amount of sodium sulphide) was suspended in boiling dry ethanol (15 ml) and to it added a solution of 2,5-dichloronitrobenzene (2·45 g) in ethanol (15 ml). After refluxing for 4 hr the cooled, dark mixture was poured into saturated sodium chloride solution (100 ml) and shaken. A brown oil which separated solidified on washing with water, and the solid was recrystallized from ethanol (15 ml) to give orange *cubes*, m.p. 138–140 °C (Found: C, 46·0; H, 2·7; N, 9·2%. Calc. for $C_{12}H_8O_2NSCl_2$: C, 45·7; H, 2·6; N, 8·9%). Yield 3·16 g, 85%. The same product was formed in lower yield and purity when the sodium salt was formed by treating pure 2-amino-4-chlorobenzenethiol with 1 equiv sodium ethoxide. Reaction of the zinc salt of the thiophenol with 2,5-dichloronitrobenzene was attempted under various conditions, but the zinc salt was always recovered unchanged.

(*d*) *2-Acetamido-4,4'-dichloro-2'-nitrodiphenyl Sulphide.*—The preceding compound (1·00 g) was dissolved in dry pyridine (3 ml) and acetic anhydride (0·5 ml) and warmed on the steam-bath for 2 hr. The cooled mixture was poured into water and the product recrystallized from ethanol (6 ml) to give 0·93 g (85%); golden-yellow, hexagonal *plates*, m.p. 167·5–168·5 °C (decomp.) (Found: N, 7·8%. Calc. for $C_{14}H_{10}O_3N_2SCl_2$: N, 7·9%).

(*e*) *2,7-Dichlorophenothiazine* (*I*).—The preceding compound (1·54 g) in dry acetone (16 ml) was treated with a solution of sodium hydroxide (173 mg) in dry ethanol (2·2 ml) and heated on the water-bath for 30 min, when a second portion of sodium hydroxide (173 mg) in ethanol was

added. After refluxing for 30 min more, most of the acetone was distilled off and the cooled mixture poured into water (80 ml). *2,7-Dichlorophenothiazine* (I) separated at once as brown needles and was recrystallized from ethanol (25 ml) to give pale fawn, long, pointed needles (1·05 g, 90%), m.p. 216–217 °C (Found: C, 54·0; H, 3·0; N, 5·1; S, 12·0; Cl, 26·4%. Calc. for $C_{12}H_7NSCl_2$: C, 53·7; H, 2·6; N, 5·2; S, 12·0; Cl, 26·5%).

(*f*) *2-Amino-5,4′-dichloro-2′-nitrodiphenyl Sulphide.*—The sodium salt of 2-amino-5-chlorobenzenethiol was condensed as in (*c*) with 2,5-dichloronitrobenzene to give *2-amino-5,4′-dichloro-2′-nitrodiphenyl sulphide* in 85% yield after purification in benzene on a column of magnesium oxide; clusters of pale brown needles from ethanol, m.p. 160 °C (decomp.) (Found: N, 9·2%. Calc. for $C_{12}H_8O_2N_2SCl_2$: N, 8·9%).

(*g*) *2-Acetamido-5,4′-dichloro-2′-nitrodiphenyl Sulphide.*—Acetylation of the preceding compound as in (*d*) gave a 90% yield, pale brown *needles* from ethanol, m.p. 159–161 °C; mixed m.p. with (*f*) <145 °C (Found: C, 47·4; H, 3·3; N, 7·7%. Calc. for $C_{14}H_{10}O_3N_2SCl_2$: C, 47·1; H, 2·8; N, 7·9%).

(*h*) *3,7-Dichlorophenothiazine* (*II*).—The preceding compound, treated as in (*e*), gave a 90% yield of *3,7-dichlorophenothiazine*, pale brown rectangular plates from ethanol, m.p. 226–227 °C (Found: C, 54·0; H, 3·0; N, 5·0%. Calc. for $C_{12}H_7NSCl_2$: C, 53·8; H, 2·6; N, 5·2%). This compound could not be made by fusion of 4,4′-dichlorodiphenylamine with sulphur, and even after fusion at 118 °C the only recognizable product was phenothiazine (cf. Mackie and Cutler (1954) who were unable to prepare chloro- and dibromophenothiazine by fusion of diphenylamines with sulphur).

(*i*) *2-Amino-5-chlorobenzenethiol* (*V*).—Freshly distilled *p*-chloroaniline (12·75 g) in glacial acetic acid (12 ml) was added dropwise at 0–10 °C under anhydrous conditions, to freshly distilled sulphur monochloride (80 g). The mixture was stirred for 4 hr, with gradual rise of temperature from 50 to 65 °C. The temperature was then raised to 80 °C for 15 min and the orange mixture rapidly darkened. Evolution of hydrogen chloride had by then almost ceased. To the cooled mixture was added dry benzene (120 ml) and the pale greenish yellow material collected, washed with benzene until free of sulphur monochloride, and dried *in vacuo* in the presence of paraffin flakes, sulphuric acid, and potassium hydroxide. The yield of the odourless Herz compound was usually quantitative, about 26 g.

The Herz compound (9·5 g) was mechanically stirred in the dark with a solution of sodium hydroxide (7·0 g) in water (70 ml) and sodium hydrosulphite (0·4 g) added. After completion of the reaction (1–1½ hr) the colourless liquid was decanted from a small amount of tar and stirred with a solution of zinc sulphate heptahydrate (7·25 g) in water (20 ml) for 5 min. Filtration gave the zinc salt of the benzenethiol which slowly darkened in air. It was rapidly washed with water containing a trace of sodium hydrosulphite and dried *in vacuo* to give 4·45 g, 55%.

Decomposition of the zinc salt with concentrated hydrochloric acid gave the hydrochloride of the amine, but the low solubility of the zinc salt required prolonged boiling and led to extensive loss. Purification of the zinc salt (Cassella and Co. 1922) was equally unsatisfactory. The zinc salt was most readily decomposed by shaking it, moistened with ethanol, with an aqueous solution of an equivalent quantity of sodium sulphide for 24 hr, and taking the filtrate to dryness under reduced pressure, using an anti-foaming stillhead. The sodium salt, formed in quantitative yield, was pure enough for direct condensations. It slowly darkened in air, but could be repurified by passing through a short column of magnesium oxide.

The free amine was obtained by treating the filtrate from the zinc salt and sodium sulphide with 6N acetic acid at 0–5 °C to give pH 7–9. The amine separated as a pale yellow solid which, after several recrystallizations from benzene, formed lemon-yellow, rectangular plates of *2-amino-5-chlorobenzenethiol*, m.p. 110–111 °C (Found: C, 45·6; H, 3·5%; S, 20·6%. Calc. for C_6H_6NSCl: C, 45·2; H, 3·8; S, 20·1%). The yield from the sodium salt was usually about 40%. The procedure of Stephens and Wibberley (1950) for preparing the zinc salt of 2-amino-5-bromobenzenethiol gave lower yields of both the Herz compound and of the zinc salt of the chloro-compound. One batch of this compound, colourless, m.p. 87 °C, when boiled with ethanol for 2 hr and recrystallized from this solvent, changed to the yellow form, m.p. 110–111 °C.

(*j*) *2-Amino-4-chlorobenzenethiol (III).*—4,4′-Dichloro-2,2′-dinitrodiphenyl disulphide (3·80 g) was dissolved in boiling, glacial acetic acid (350 ml) and to the solution at 100 °C was added zinc dust (20 g) over 30 min. The mixture was boiled for 10 min and the cloudy solution decanted. The residue was extracted with boiling acetic acid (2 × 50 ml), then with boiling water (100 ml) and the extracts added to the solution, and boiling water (800 ml) added. After standing overnight in the refrigerator the zinc salt (3·1 g, 80%) separated. It was converted almost quantitatively to the sodium salt as in (*i*) and neutralization of the sodium salt gave a low yield of *2-amino-4-chlorobenzenethiol* as lemon-yellow, elongated hexagonal plates from benzene, m.p. 119–121 °C (Found: C, 45·6; H, 3·6; N, 8·6; S, 20·7; Cl, 22·8%. Calc. for C_6H_6NSCl: C, 45·2; H, 3·8; N, 8·8; S, 20·1; Cl, 22·2%).

(*k*) *2-Amino-3,5-dichlorobenzenethiol.*—Application of the Herz reaction as in (*i*) to *o*-chloroaniline gave, ultimately, long, lemon-yellow *needles* from ethanol, m.p. 95 °C, soluble in 3N hydrochloric acid and slowly soluble in 10% sodium hydroxide solution (Found: N, 6·9; S, 16·6; Cl, 36·1%. Calc. for $C_6H_5NSCl_2$: N, 7·2; S, 16·5; Cl, 36·6%). Yields at all stages were much lower than in (*i*).

(*l*) *2-Amino-3,5,4′-trichloro-2′-nitrodiphenyl Sulphide.*—Condensation of the sodium salt of the preceding compound (obtained from the zinc salt) with 2,5-dichloronitrobenzene as in (*c*), gave *2-amino-3,5,4′-trichloro-2′-nitrodiphenyl sulphide* in 20% yield; pale brown cubes from ethanol, m.p. 155–158 °C (Found: N, 8·0; Cl, 30·4%. Calc. for $C_{12}H_7O_2N_2SCl_3$: N, 8·0; Cl, 30·5%).

(*m*) o-*Acetamidobenzenethiol.*—Acetylation of *o*-aminobenzenethiol (b.p. 80–84 °C/3 mm) (Kiprianov, Ushenko, and Gershun 1944) dissolved in 3 times its volume of glacial acetic acid, with its own weight of acetic anhydride, for 5 min and without external heating, gave a small and variable yield of *o-acetamidobenzenethiol*, as a tough mat of fine, colourless needles from ethanol, m.p. 114·5–115·5 °C (Found: C, 57·1; H, 5·6%. Calc. for C_8H_9ONS: C, 57·5; H, 5·4%).

(*n*) *2,2′-Diacetamidodiphenyl Disulphide.*—Oxidation of *o*-aminobenzenethiol (Teppema and Sebrell 1927) gave 2,2′-diaminodiphenyl disulphide, m.p. 90–91 °C without recrystallization, in 90% yield. This, dissolved in glacial acetic acid (5 ml/g) was acetylated on the water-bath for 1 hr with twice its weight of acetic anhydride to give *2,2′-diacetamidodiphenyl disulphide* as colourless needles from ethanol in 80% yield, m.p. 166–167 °C (Found: C, 57·5; H, 4·9; N, 8·2%. Calc. for $C_{16}H_{16}O_2N_2S_2$: C, 57·8; H, 4·9; N, 8·4%).

V. Acknowledgment

The authors thank Dr. J. Cymerman-Craig for discussions during the course of this work.

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A NEW SESQUITERPENE ALCOHOL FROM *HIMANTANDRA BACCATA* BAIL.

By A. J. Birch* and K. M. C. Mostyn*

[*Manuscript received April* 15, 1955]

Summary

A new crystalline sesquiterpene alcohol has been isolated from the bark of *Himantandra baccata* Bail. (syn. *Galbulimima baccata*). It is a tricyclic saturated *tert.*-alcohol, $C_{15}H_{26}O$, which yields guaiazulene on dehydrogenation. The formulae I and II are suggested as possibilities.

I. Introduction

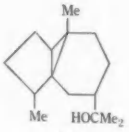
Solvent extraction of the milled bark of *Himantandra baccata* Bail. has yielded a number of compounds including an essential oil consisting largely of sesquiterpene derivatives (Hughes and Ritchie personal communication). Fractionation of the oil gave a considerable proportion of material, b.p. *c.* 100 °C/0·05 mm, which partly solidified. The purified material, himbaccol, $C_{15}H_{26}O$, has m.p. 76°C, $[\alpha]_D$ −10° (ethanol) and does not appear to be a known compound. It is saturated, gives no colour with tetranitromethane, cannot be hydrogenated at atmospheric pressure over palladium-charcoal, and resists the action of ozone, perbenzoic acid, and potassium permanganate in acetone. It must therefore be tricyclic. The infra-red spectrum, kindly examined by Dr. A. R. Cole, has a band at 2·95 μ indicative of the presence of an hydroxyl group. It was recovered unchanged after treatment with phthalic anhydride in boiling benzene, with 3,5-dinitrobenzoyl chloride in pyridine or with chromium trioxide in pyridine (Poos *et al.* 1953); heating with mineral acid under mild conditions resulted in dehydration. It must therefore be a *tert.*-alcohol.

Oxidation of himbaccol with chromic acid in acetic acid (Fieser 1948) gave rise to acetone and a ketone, $C_{12}H_{18}O$, isolated as their 2,4-dinitrophenylhydrazones. The tertiary hydroxyl group is therefore associated with the *iso*propyl group in the manner shown either in I or II.

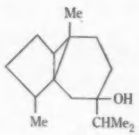
Himbaccol readily produced guaiazulene (1,4-dimethyl-7-*iso*propylazulene) on dehydrogenation with palladium-charcoal. It would therefore appear that one of the rings is very readily opened and is probably three-membered. The position of the ring is conjectural. Infra-red data show that a *cyclo*propane ring, if present, does not contain a methylene group (Cole personal communication). Furthermore, it probably does not terminate in a position adjacent to the *iso*propyl side-chain, since the 2,4-dinitrophenylhydrazone of the C_{12}-ketone

* Department of Organic Chemistry, University of Sydney.

is stable to acid under conditions where the derivative of thujone is readily converted to that of *iso*thujone. Structures I or II are suggested as working hypotheses.



(I)



(II)

II. Experimental

(*a*) *Isolation.*—Crude himbaccol, kindly presented by Dr. G. K. Hughes and Dr. E. Ritchie, was drained on a porous tile. It was then chromatographed in light petroleum (b.p. 40–60 °C) on alumina (40 times its weight). Elution was with light petroleum with increasing admixture of ether up to equal volumes. Himbaccol appeared in the initial fractions, the later ones being contaminated by a liquid alcohol. Crystallization from aqueous methanol raised the m.p. to 76 °C. The action of potassium permanganate in cold acetone for 12 hr gave a more readily purified product (Found: C, 81·1; H, 11·8%. Calc. for $C_{15}H_{26}O$: C, 81·0; H, 11·8%).

(*b*) *Dehydrogenation.*—The alcohol (1·0 g) was heated at 225–235 °C for 2 hr with palladium-charcoal (10%) (cf. Linstead and Thomas 1940). The product was taken up in light petroleum (b.p. 40–70 °C) and chromatographed on alumina (35 g), the deep blue azulene band and the fraction immediately preceding it being collected separately. The latter fraction showed no signs of reaction with 2,4,6-trinitrobenzene (lack of cadalene) but the azulene readily gave an almost black complex. This was boiled several times with hexane and the undissolved residue recrystallized from methanol. It formed almost black needles, m.p. 149·5–150 °C, undepressed by an authentic specimen of the derivative of guaiazulene m.p. 150–151 °C.

(*c*) *Oxidation.*—To himbaccol (2 g) in pure acetic acid (15 c.c.) was added powdered chromium trioxide (1·1 g) in three portions over 1 hr with stirring, which was continued for a further 3 hr. Water (80 c.c.) was added and the mixture slowly distilled, the first 2 c.c. of distillate being added to 2,4-dinitrophenylhydrazine in 2N hydrochloric acid. The yellow derivative, m.p. 110–115 °C, was passed through alumina in benzene and crystallized from ethanol to give acetone 2,4-dinitrophenylhydrazone (145 mg), m.p. 123–124 °C undepressed by an authentic specimen m.p. 124 °C. The aqueous-acetic acid solution from the original oxidation was extracted with ether, the extract washed with aqueous sodium hydroxide, dried, and evaporated to give a sweet-smelling oil. This gave rise to a crystalline bisulphite compound, decomposed with dilute HCl. The oil so obtained (95 mg) gave a pale yellow 2,4-dinitrophenylhydrazone, crystallized from methanol, m.p. 94–95 °C (Found: C, 60·0; H, 6·3%. Calc. for $C_{18}H_{22}O_4N_4$: C, 60·3; 6·1%). Brief heating on the steam-bath with ethanolic sulphuric acid (10%) did not change this derivative.

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ALKALOIDS OF THE AUSTRALIAN RUTACEAE: *EVODIA XANTHOXYLOIDES* F. MUELL.

V. A NOTE ON THE CONSTITUTION OF EVOLIDINE

By F. W. Eastwood,* the Late G. K. Hughes,* and E. Ritchie*

WITH X-RAY STUDY†‡

By R. M. Curtis§

[*Manuscript received May* 10, 1955]

Summary

Evolidine, formerly described as an alkaloid, is shown to be a peptide. A new formula $C_{38}H_{58}O_9N_8$ having a cyclic structure and containing seven amino acid residues is proposed.

I. Introduction

The investigation of the relationships between amino acids, peptides, and proteins has advanced rapidly over the last few years and the general situation has been periodically reviewed (Khorana 1952; Elliott 1953; Hughes and Sinex 1954; Tristram 1954). Structural work has mainly centred on materials arising from bacterial and animal sources but the nitrogen metabolism of the higher plants has also been actively investigated (Wood 1953). The value of peptides as model compounds for the elucidation of the relationship between the structure and the physicochemical properties of the proteins is apparent in the recent solutions of the structures of several peptides. These advances, however, are hampered by the relative scarcity of these compounds (Synge 1949; Bricas and Fromageot 1953) and the isolation of a new highly crystalline neutral peptide from a botanical source is therefore of considerable interest.

In Part II of this series (Hughes, Neill, and Ritchie 1952) the isolation of the alkaloidal constituents of the leaves of *Evodia xanthoxyloides* F. Muell. was described. In subsequent parts (Cannon *et al.* 1952; Eastwood, Hughes, and Ritchie 1954) the alkaloids have been shown to fall into the acridone and furoquinoline classes. In addition to these a minor colourless nitrogenous compound, formerly considered to be an alkaloid and named evolidine, was obtained.

* Department of Organic Chemistry, University of Sydney.

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§ California Institute of Technology, Pasadena, Cal.; present address: Shell Development Co., Emeryville, Cal.

II. The Structure of Evolidine

Evolidine is a colourless optically active neutral or very weakly basic compound. The material used was isolated from the leaves of *E. xanthoxyloides* (Hughes, Neill, and Ritchie 1952) and was purified by the conventional procedure of recrystallization from acetone, ethanol, and aqueous methanol to constant melting point and rotation and apparent homogeneity by paper chromatography using butanol-water-acetic acid (4 : 1 : 1) and developing with iodine. It is well known that the classical criteria of purity in compounds of the peptide type are of little value but these considerations have generally applied to water-soluble acidic or basic compounds isolated from complex aqueous extracts. However, evolidine, although hydrated, is insoluble in water, neutral, and highly crystalline. In addition, the method of isolation and the evidence obtained from the X-ray investigation indicated that our preparation of evolidine was a pure compound.

Evolidine is quite insoluble in aqueous alkali, soluble in 10N hydrochloric acid, but not appreciably soluble in less concentrated acid. Examination of the acid hydrolysis products by two-dimensional paper chromatography showed the presence of six different α-amino acids, namely, aspartic acid, leucine or *iso*leucine, phenylalanine, proline, serine, and valine. Ammonia was also isolated as ammonium chloride.

The empirical formula and molecular weight calculated for a cyclic peptide structure containing these six amino acids with ammonia present as amide (asparagine or *iso*asparagine residue) do not agree with the empirical formula obtained from chemical analysis and the molecular weight obtained from X-ray crystal analysis. Although no quantitative analyses of the amino acids and ammonia have as yet been attempted, the inclusion of a second leucine or *iso*-leucine residue in the cyclic structure gives an empirical formula $C_{38}H_{58}O_9N_8$, mol. wt. 771, in good agreement with the analytical data and the X-ray mol. wt. 769 ± 6.

The formula proposed above, having a cyclic structure containing seven amino acid residues, was confirmed by the analysis and molecular weight obtained for the hydrate which contained four molecules of water $C_{38}H_{58}O_9N_8.4H_2O$, mol. wt. 833 in agreement with the value found 837 ± 4. In addition the presence in the molecule of 1 molecule of serine necessitates the existence of a free hydroxyl group. The presence of this group has been confirmed by the formation of an *O*-acetyl derivative, $C_{40}H_{60}O_{10}N_8$, which is readily reconverted to evolidine by dilute acid hydrolysis. The formation of an *O*-acyl derivative only, even on vigorous treatment with acetic anhydride, indicates the absence of a free amino group.

III. X-Ray Investigation of Evolidine

Crystals of good optical quality were obtained by slow crystallization from aqueous methanol to which a small amount of butyl acetate had been added. The crystals show a pronounced tendency to twin with (001) as the twinning plane, but single crystals also occur.

The density of evolidine was determined by flotation in a chlorobenzene-bromobenzene solution; it was found to be $1 \cdot 276 \pm 0 \cdot 004$ g/c.c. All X-ray photographs were taken on a precession camera the radius of which had been calibrated with a crystal of sodium chloride as reference substance. The films were corrected for shrinkage by means of fiducial marks placed on the films during photography.

The determination of the space group and the choice of axes were made on the basis of precession photographs of several zero-level nets containing the a^*-axis. The symmetry was found to be triclinic and the space group P1, the space group $P\bar{1}$ being ruled out on the basis of the optical activity of the peptide. The dimensions of the unit cell are given below; errors are expressed as standard deviations.

$$a_0 = 9 \cdot 12 \pm 0 \cdot 04 \qquad \alpha = 107^\circ\ 15' \pm 7'$$
$$b_0 = 11 \cdot 41 \pm 0 \cdot 05 \qquad \beta = 94^\circ\ 36' \pm 10'$$
$$c_0 = 11 \cdot 80 \pm 0 \cdot 05 \qquad \gamma = 68^\circ\ 27' \pm 10'$$
$$V = 1089 \pm 4 \text{A}^3 \quad \text{cell mass} = 837 \pm 4.$$

The percentage of water was determined in crystals taken from the same crystallization batch as that which provided the crystals used for the X-ray work. A sample was dried to constant weight over phosphorus pentoxide *in vacuo* successively at 25, 56, 76, and 100 °C. A sample of 6·245 mg showed successive losses of 0·413 mg (25 °C, 9 hr), 0·070 mg (56 °C, 6 hr), 0·000 mg (76 °C, 3 hr), and 0·024 mg (100 °C, 6 hr), making a total loss of 0·570 mg or 8·12 per cent.

Subtracting 8·12 per cent. of 837 (=68) from the cell mass leaves 769 ± 6 as the molecular weight of the peptide.

IV. Experimental

Melting points are uncorrected. Analyses are by Dr. K. W. Zimmermann, C.S.I.R.O. Microanalytical Laboratory.

(*a*) *Properties of Evolidine.*—Evolidine is readily soluble in methanol and ethanol, slightly soluble in acetone, but insoluble in water or chloroform. It was purified by repeated crystallization from acetone or absolute ethanol from which it crystallized in colourless needles. Crystallization from aqueous methanol or ethanol gave colourless prisms of the hydrated form. Both forms of evolidine had m.p. 277–279 °C. Optical rotations taken on the hydrated material whose formula was more readily defined by analysis, were $[\alpha]_D^{13^\circ}$ −127° (*c*, 0·47 in ethanol) and $[\alpha]_D^{16^\circ}$ −129° (*c*, 0·45 in ethanol). After prolonged drying at 118 °C *in vacuo* the material was extremely hygroscopic (Found: C, 58·9; H, 7·5; N, 13·9%. Calc. for $C_{38}H_{58}O_9N_8$: C, 59·2; H, 7·6; N, 14·5%). The hydrated material was analysed after drying at room temperature *in vacuo* (Found: C, 54·9; H, 7·9; N, 13·1%. Calc. for $C_{38}H_{58}O_9N_8.4H_2O$: C, 54·8; H, 8·0; N, 13·4%). Evolidine is insoluble in dilute acid or alkali but is soluble in concentrated hydrochloric acid.

(*b*) *Acetyl Evolidine.*—Evolidine (0·2 g), anhydrous sodium acetate (0·2 g), and acetic anhydride (4 ml) were heated on the water-bath for 4 hr, the mixture poured into water, and the product collected. It crystallized from aqueous methanol in colourless needles, m.p. 248–250 °C, readily soluble in cold chloroform (Found: C, 58·8; H, 7·6; O, 19·7; N, 13·5%. Calc. for $C_{40}H_{60}O_{10}N_8$: C, 59·1; H, 7·4; O, 19·7; N, 13·8%). Hydrolysis of this material with dilute methanolic hydrochloric acid for 1 hr on the steam-bath gave, on diluting with water, a product which crystallized from aqueous methanol in colourless prisms, m.p. and mixed m.p. with evolidine 277–279 °C.

(c) *Hydrolysis of Evolidine.*—Evolidine (0·1 g) was hydrolysed with hydrochloric acid (5 ml of 6N) for 12 hr under reflux and the excess acid removed under vacuum at room temperature. The residue was examined by two-dimensional paper chromatography using butanol-water-acetic acid (4 : 1 : 1) followed by phenol containing 20% water on Whatman No. 1 papers treated with ethylenediaminetetra-acetic acid. The amino acids were identified by comparison with authentic specimens after developing with ninhydrin. Proline was additionally identified by development of the blue colouration when treated with isatin.

Evolidine (0·4 g) was hydrolysed in the same manner, then the solution made alkaline with sodium hydroxide and distilled into hydrochloric acid. The resulting solution was evaporated to dryness when the colourless crystalline residue was collected. It was purified by sublimation at the ordinary pressure (Found : N, 25·9%. Calc. for NH_4Cl : N, 26·2%).

V. Acknowledgments

The authors are indebted to Dr. T. Reynolds, C.S.I.R.O., for advice and assistance in the identification of the amino acids.

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THE ALKALOIDS OF *ERECTITES QUADRIDENTATA* D.C.

By C. C. J. CULVENOR* and L. W. SMITH*

[*Manuscript received April 22, 1955*]

Summary

Senecionine, seneciphylline, and retrorsine have been isolated from *Erectites quadridentata* D.C. where they occur mainly in the form of their *N*-oxides. The alkaloids, hieracifoline and pterophine, are shown to be mixtures of senecionine and seneciphylline.

I. INTRODUCTION

The genus *Erectites* is closely related to *Senecio* but alkaloids from only one species, *E. hieracifolia*, have been reported in the literature. From this species Manske (1939) isolated two bases, $C_{18}H_{25}O_5N$ and $C_{20}H_{17}O_6N$, and the former, named hieracifoline, was shown by hydrolysis to retronecine and a dibasic acid to be a typical pyrrolizidine alkaloid. *Erectites quadridentata* D.C. is widespread in Victoria and a study of its alkaloids has been made as an aid to assessing its potential danger to stock. It occurs in both tomentose and glabrous varieties and the present paper is concerned with the former.

Preliminary assay disclosed that the alkaloids were present mainly in the form of *N*-oxides. Reduction of the aqueous acid solution of total base, increased the amount of base isolated by chloroform extraction from 0·01 to 0·10 per cent. dry weight. Paper chromatography in butanol-acetic acid showed the crude base to consist of a major component R_F 0·56 and two minor components R_F 0·50 and 0·38. Crystals separated readily from ethanol but the product was a mixture of the two higher R_F bases. This mixture proved difficult to resolve and recrystallization, chromatography on alumina, and chromatography on powdered cellulose columns, were all ineffective. Although the bases were separated on paper sheets by butanol-acetic acid, in the cellulose column procedure with the same solvent, both were eluted together close to the solvent front. A good separation was finally achieved by use of a partition column composed of powdered Pyrex glass supporting a buffer of pH 4·0. A mixture of carbon tetrachloride (60 per cent.) and chloroform eluted a base, $C_{18}H_{25}O_5N$, $[\alpha]_D$ −55·4° (*c*, 1·0 in chloroform), m.p. 243·5–244·5 °C, while chloroform eluted the second component, $C_{18}H_{23}O_5N$, $[\alpha]_D$ −134° (*c*, 1·0 in chloroform), m.p. 216·5–217 °C. By direct comparison with authentic samples (mixed melting point, paper chromatography, infra-red absorption), the former, R_F 0·56, was identified as senecionine, and the latter, R_F 0·50, as seneciphylline (α-longilobine). On alkaline hydrolysis, both bases yielded retronecine and the appropriate acid, senecic acid and *iso*seneciphyllic acid, respectively.

* Division of Industrial Chemistry, C.S.I.R.O., Melbourne.

The minor base, R_F 0·36, was isolated from mother liquors (or subsequently directly from crude total base) by chromatography on alumina. After purification, this base had m.p. 216–216·5 °C, $[\alpha]_D^{20}$ −62·4° (chloroform), and comparison with an authentic sample showed it to be identical with retrorsine. Adams and Govindachari (1949*b*) and Warren *et al.* (1950) quote −49° as being the most reliable figure for the specific rotation of retrorsine but the lowest laevorotation recorded for any sample of the *E. quadridentata* base was −61°. No evidence was found to indicate contamination of our samples by riddelliine ($[\alpha]_D$ −109°), a difficulty separable congener of retrorsine in some *Senecio* species

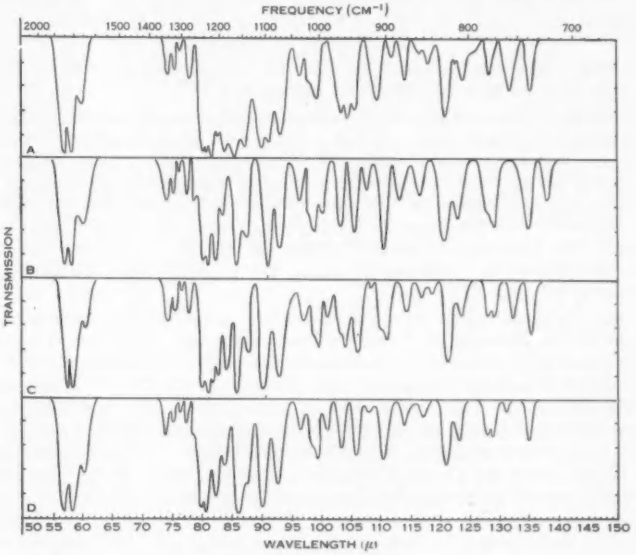

Fig. 1.—Infra-red spectra.

A, Senecionine;
B, Seneciphylline;
C, Hieracifoline;
D, Pterophine.

(Adams and Govindachari 1949*b*). Artificial mixtures of retrorsine and riddelliine were found to be almost completely resolved on a partition column of glass powder and pH 6·0 buffer, but our sample of retrorsine was not essentially changed in rotation after subjection to this procedure. The retrorsine, which was kindly supplied by the Director of Veterinary Services, Onderstepoort, was found to have m.p. 217–218 °C, $[\alpha]_D^{20}$ −58° (*c*, 1 in chloroform). We have found retrorsine containing a small amount of senecionine to melt as high as 219–220 °C.

The marked similarity between the properties of the senecionine-seneciphylline mixture from *E. quadridentata* and those reported for hieracifoline

(Manske 1939) and the base pterophine, isolated by de Waal (1940) from *Senecio pterophorus* and *S. ilicifolius*, prompted an examination of these two substances. As disclosed in a previous note (Culvenor and Smith 1954), both substances were found to be mixtures of senecionine and seneciphylline. On a paper chromatogram, both showed two spots of R_F 0·58 and 0·52, and the resolution of pterophine into its two components is described in Section II. The infra-red absorption spectra of hieracifoline and pterophine, which confirm this result, are reproduced in Figure 1, together with those of senecionine and seneciphylline. The sample of pterophine available to us had a higher laevorotation than that recorded by de Waal, due apparently to a higher proportion of seneciphylline.

II. Experimental

All melting points were performed in evacuated Pyrex capillaries. Microanalyses were carried out by the C.S.I.R.O. Microanalytical Laboratory.

(*a*) *Preliminary Assay.*—Dried, milled, whole plant (200 g) was extracted with hot methanol, and the extract concentrated under reduced pressure until all methanol was removed. The residue was extracted with 2% hydrochloric acid and this extract (310 ml) divided into two equal parts. One part was further acidified with sulphuric acid (11 ml) shaken for 4 hr with zinc dust (20 g) and then filtered. Both parts were made alkaline to phenolphthalein with ammonia and separately extracted with chloroform. The resulting crude "unreduced" and "reduced" base fractions were made up to a standard volume and aliquots were titrated with *p*-toluenesulphonic acid in chloroform. Assuming an average mol. wt. of 350, the results indicated 0·01% free base and 0·09% base *N*-oxide.

(*b*) *Isolation of Crude Base.*—The crude base (48·2 g crystalline solid) was isolated from the whole plant (70 lb) similarly to the "reduced" base in the assay procedure, the whole of the dilute acid extract being reduced with zinc and sulphuric acid. Crystallization of the base from a large volume of ethanol gave colourless crystals (26 g), m.p. 229–230 °C. Evaporation of the mother liquors gave a brown gum (25 g) which on rubbing with cold ethanol yielded additional crystalline material (6 g). Both the crystals and the residual gum gave spots of R_F 0·56, 0·50, and 0·38 on a paper chromatogram. Repeated recrystallization of the solid from ethanol gave a product of m.p. 243·5–244 °C, which was shown by paper chromatogram to be almost pure senecionine with a trace of seneciphylline, but the amount obtained was very small.

(*c*) *Paper Chromatography.*—The developing solvent was the upper phase resulting from shaking butanol with an equal volume of 5% aqueous acetic acid. The tank was lined with paper wetted with the aqueous phase and an equilibrating period of at least 3 hr, before beginning the solvent run, was essential for obtaining a good separation of senecionine and seneciphylline.

(*d*) *Chromatography on Alumina.*—Crude total base (2·2 g) was applied to a column of alumina (35 g) from chloroform solution. Chloroform and 50% chloroform-methanol eluted mixtures of the two high R_F components (1·9 g), while methanol eluted the base R_F 0·38 (0·2 g). The remaining crude base was separated similarly into mixed high R_F bases (16·6 g) and base R_F 0·38 (1·92 g), and these two fractions were then used as starting material for the isolations described below.

(*e*) *Isolation of Senecionine and Seneciphylline.*—Chromatography of the mixed high R_F bases on kieselguhr-phosphate buffer columns was tried without success. At pH 6·2, very little separation occurred, while at pH 3·9 there was evidence of decomposition, the recovered base showing extra spots of R_F 0·64, 0·16, and 0·06.

With Pyrex glass (passing 200 mesh) as carrier for the buffer phase, no decomposition took place and a satisfactory separation was achieved. This glass had an acid surface reaction which was not eliminated by warming with sodium carbonate solution, washing, and drying, and although suitable for the present purpose is not suitable as a carrier for alkaline buffers.

Glass powder (1700 g) was mixed by grinding in a mortar with potassium phosphate buffer (pH 4·0, *d* 1·1; 300 ml) and packed, as a slurry in light petroleum, into a column 90 by 5 cm.

The mixed bases (2·5 g of R_F 0·56, 0·50 only) were applied in solution in carbon tetrachloride containing 20% chloroform. Eluting solvents and products obtained are detailed in Table I.

The product from fractions 13–30 was twice recrystallized from ethanol to give senecionine as colourless plates, m.p. 244–245 °C, $[\alpha]_D^{20}$ —55·4° (*c*, 1·0 in chloroform) (Found : C, 64·5; H, 7·5; N, 4·3; O, 23·8%. Calc. for $C_{18}H_{25}O_5N$: C, 64·5; H, 7·5; N, 4·2; O, 23·9%). A mixture with an authentic sample of senecionine of m.p. 240–241 °C, also melted at 240–241 °C.

Crystallization from ethanol of the base from fractions 31–34 gave small colourless prisms of seneciphylline, m.p. 215–216 °C, $[\alpha]_D^{20}$ —125° (*c*, 1 in chloroform). From the rotation it was evident that this sample still contained a small proportion of senecionine and 1·5 g of material obtained similarly was rechromatographed on a fresh column. The appropriate fraction, after recrystallization from ethanol gave prisms, m.p. and mixed m.p. 216·5–217 °C, $[\alpha]_D^{20}$ —134° (*c*, 1·0 in chloroform) (Found : C, 64·8; H, 7·1; N, 4·3; O, 24·0%. Calc. for $C_{18}H_{23}O_5N$: C, 64·9; H, 6·9; N, 4·7; O, 24·0%).

TABLE 1

CHROMATOGRAPHY OF SENECIONINE-SENECIPHYLLINE MIXTURE ON PYREX GLASS

pH 4·0 buffer

Fraction	Eluant	Volume (l.)	Residue Wt. (g)	R_F Value	D (in $CHCl_3$)	M.P. (°C)
1–12	80/20 $CCl_4/CHCl_3$	3	—	—	—	—
13–29	60/40 $CCl_4/CHCl_3$	16	2·0	0·58	—60	243–244
30	$CHCl_3$	1	0·16	0·58	—60	243–244
31–34	$CHCl_3$	5	0·39	0·52	—125	216–217

(*f*) *Isolation of Retrorsine.*—The base R_F 0·38 fraction, twice recrystallized from acetone, had m.p. 219–220 °C, $[\alpha]_D^{20}$ —61·4° (*c*, 1 in chloroform). To remove a small amount of the higher R_F bases, this material (1·0 g) was applied to a 70 by 2·5 cm column packed with Pyrex glass (310 g) and phosphate buffer (pH 6·5, *d* 1·1; 55 ml). A 60% carbon tetrachloride-chloroform mixture (650 ml) eluted base of R_F 0·57 (0·13 g) and chloroform (1 l.) the base of R_F 0·38 (0·75 g). From acetone, the latter fraction yielded retrorsine as colourless prisms, m.p. and mixed m.p. 216–216·5 °C, $[\alpha]_D^{20}$ —62·4° (*c*, 1·0 in chloroform) (Found : C, 61·8; H, 7·1; N, 3·9; O, 27·3%. Calc. for $C_{18}H_{25}O_6N$: C, 61·5; H, 7·1; N, 4·0; O, 27·4%). The infra-red absorption and R_F value were identical with those of authentic retrorsine.

(*g*) *Hydrolysis of the Bases.*—(i) *Senecionine.* The base (1 g) and barium hydroxide (2 g) were refluxed in water (14 ml) for 2 hr. After saturating with carbon dioxide, the solution was filtered, acidified to congo red, and extracted continuously with ether. The ether extract yielded a gum (0·46 g) which from ethyl acetate-light petroleum gave prisms, m.p. 145·5–146 °C, $[\alpha]_D^{20}$ +11·7° (*c*, 0·5 in ethanol) (Found : C, 55·8; H, 7·6; O, 36·3%. Calc. for $C_{10}H_{16}O_5$: C, 55·6; H, 7·4; O, 37·0%). A solution of this acid in conc. hydrochloric acid was evaporated to dryness, the process repeated, and the product crystallized from benzene to give the lactone, m.p. 155–156 °C (Found : C, 60·5; H, 7·0%. Calc. for $C_{10}H_{14}O_4$: C, 60·6; H, 7·1%). Senecic acid and its lactone are reported to have m.p. 146 °C, $[\alpha]_D^{25}$ +10·95° (*c*, 3 in ethanol) and m.p. 156 °C respectively (Adams and Govindachari 1949*a*). The residual hydrolysis solution was basified with sodium hydroxide and evaporated to dryness. The residue, extracted with ethanol gave crystals (0·18 g), forming prisms from acetone, m.p. 118–119 °C, $[\alpha]_D^{22}$ +53·9° (*c*, 1 in ethanol) (Found : C, 61·9; H, 8·9; N, 9·0; O, 21·2%. Calc. for $C_8H_{15}O_2N$: C, 61·9; H, 8·4; N, 9·0; O, 20·6%). From this base was prepared the hydrochloride, m.p. 163–164 °C, which did not depress the m.p. of authentic retronecine hydrochloride of m.p. 161 °C.

(ii) *Seneciphylline.* Hydrolysis of this base (0·5 g) by a similar procedure yielded *iso*senecic phyllic acid (0·27 g), m.p. 115–116 °C (from ethyl acetate-light petroleum), $[\alpha]_D^{20}$ 0·0° (*c*, 1·0 in ethanol) (Found: C, 56·2; H, 6·6; O, 37·0%. Calc. for $C_{10}H_{14}O_5$: C, 56·1; H, 6·5; O, 37·4%), and retronecine, m.p. and mixed m.p. 116–117 °C).

(iii) *Retrorsine.* The acidic product from the hydrolysis of base R_F 0·38 (0·5 g) yielded from ethyl acetate-light petroleum crystals, m.p. 147·5–148 °C (isatinecic acid, m.p. 147·5 °C), and from the mother liquors a substance, m.p. 150–151·5 °C, $[\alpha]_D^{20}$ +20·3° (*c*, 0·5 in water), probably a mixture of isatinecic acid and its lactone (see Christie *et al.* 1949). From the basic product was obtained retronecine, m.p. and mixed m.p. 116–117 °C.

(*h*) *Separation of Retrorsine and Riddelliine.*—A mixture of retrorsine (11·3 mg) and riddelliine (10·3 mg) was applied to a column (1·4 by 34 cm) packed with Pyrex glass powder (48 g) and potassium phosphate buffer (pH 6·0, *d* 1·1; 8 ml). Eluting solvents were 60% carbon tetrachloride-chloroform (100 ml), 40% carbon tetrachloride-chloroform (90 ml), 30% carbon tetrachloride-chloroform (150 ml), and chloroform (60 ml). Fractions of 5 ml were collected and the amount of base present determined by titration. The titration curve showed a fairly sharp retrorsine peak at tubes 38–47 (10·0 mg base, R_F 0·39), a small mixed portion at tubes 48–49 (1·0 mg base, R_F 0·39, 0·32), and a low riddelliine peak at tubes 50–70 (9·6 mg base, R_F 0·32). This represents a recovery of 88% of the retrorsine and 93% of the riddelliine in an essentially pure state. The use of kieselguhr (" Hyflo Supercel ") instead of glass powder as carrier gave almost as good results, but elution with benzene-chloroform mixtures in place of the solvents used above gave a poorer separation.

(*i*) *Isolation of Senecionine and Seneciphylline from Pterophine.*—Pterophine (0·38 g) was applied to a 90 by 5 cm column packed with Pyrex glass powder (310 g) and potassium phosphate buffer (pH 4·0, *d* 1·1; 55 ml). The solvents used and products obtained are shown in Table 2

TABLE 2

FRACTIONATION OF PTEROPHINE ON PYREX GLASS POWDER

pH 4·0 buffer

Fraction	Eluant	Volume (l.)	Product Wt. (g)	R_F Value
1–14	60/40 $CCl_4/CHCl_3$	3·4	0·16	0·58, 0·51
15–25	" "	3·4	0·17	0·51
16–27	$CHCl_3$	1·0	0·05	0·51

This column did not effect as good a separation as in previous cases although fractions 15–27 yielded pure seneciphylline, m.p. 216–217 °C after crystallization from ethanol. Fraction 1–14 was run on a second column and in this case 60% carbon tetrachloride-chloroform (5 l) eluted essentially pure senecionine (0·08 g), m.p. and mixed m.p. 241–242 °C, while chloroform eluted the seneciphylline (0·08 g), m.p. 215–216 °C, mixed m.p. 216–217 °C.

(*j*) *Infra-red Absorption Spectra.*—The spectra in Figure 1 are for the crystalline substances in " Nujol " mulls and the region of absorption by " Nujol " is therefore omitted. Adams and Govindachari (1949*b*) considered the band at 757 cm^{-1} to be characteristic of senecionine and those at 902, 992 cm^{-1} characteristic of seneciphylline.

III. ACKNOWLEDGMENTS

The authors are indebted to Dr. J. B. Willis for the infra-red spectra, to Dr. R. H. F. Manske for a sample of hieracifoline, to the Director of Veterinary Services, Onderstepoort, South Africa, for samples of pterophine and retrorsine, Professor R. Adams for a sample of riddelliine, and Professor F. L. Warren for a sample of retrorsine.

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SHORT COMMUNICATIONS

THE DIPOLE MOMENT OF ACENAPHTHENE*

By J. Y. H. Chau† and R. J. W. Le Fèvre†

The M.I.T. Tables (Wesson 1948) list the moment of acenaphthene as 1·5–1·6 D, an estimate based upon measurements made by Lumbroso (1947) on solutions in benzene or dioxan and apparently inspired by the theory of Coulson and Rushbrook (1940). However, elementary principles suggest that the polarity of acenaphthene would be about double that of toluene (namely, *c.* twice 0·37 D, McAlpine and Smyth 1933 ; Baker and Groves 1939). Subsequently the original high figure has been twice reduced, first to 0·97 D (in benzene, Lumbroso 1949) and then to 0·85 D (in benzene, Bergmann, Fischer, and Pullman 1951). No repetition has yet been reported of Lumbroso's determination in dioxan. The present note provides this and also adds new data relating to carbon tetrachloride as solvent.

Experimental

The acenaphthene used had m.p. 96·0 °C (Beilstein's *Handbuch*, V, E II, p. 495, gives 96·2 °C). Dioxan (A.R. grade) was dried over sodium, fractionated (b.p. 100–101 °C), and stored over sodium (cf. Blout and Fields 1948). Carbon tetrachloride was as described by Le Fèvre and Le Fèvre (1954). Observations of dielectric constants ε and densities d are given in Table 1 against concentrations expressed as weight fractions w. Subscripts 12, 1, or 2 indicate solution, solvent, or solute respectively. Experimental techniques and methods of calculation were as noted by Le Fèvre (1953).

The total polarizations, ${}_\infty P_2$, of acenaphthene at infinite dilution emerge via,

$$ {}_\infty P_2 = M_2[p_1(1-\beta)+C\alpha\varepsilon_1] $$

(cf. Le Fèvre 1953) as 65·1 c.c. in carbon tetrachloride and 64·5 c.c. in dioxan. The molecular refraction, R_D, for Na-D light follows from the observations of von Auwers and Frühling (1921) on the molten hydrocarbon as 51·93 c.c. Kikina, Schott-'Lvova, and Syrkin (1954) have recently given higher values ranging from 56·1 c.c. for light of λ=4046·6 A to 52·03 c.c. for λ=6439·5 A. We have not utilized these, however, since the text of the Russian paper has not yet been seen by us. Their effect would be to lower slightly the polarity estimates which follow. In any case, R_D is only an approximation for the distortion polarization. Taking the last-named as 51·9 c.c. we obtain :

$\mu = 0{\cdot}8_0$ D in carbon tetrachloride,
$\mu = 0{\cdot}7_9$ D in dioxan.

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† School of Chemistry, University of Sydney.

An attempt has also been made to measure μ_{gas}. Unfortunately an adequate pressure of acenaphthene was only secured at temperatures near the upper limit of usefulness of the apparatus now available (cf. Le Fèvre and Rao 1954, 1955*a*, 1955*b*). The standardizing dielectric was air for which a temperature invariant polarization of 4·34 c.c. (corresponding to $\varepsilon=1{\cdot}000582$ at N.T.P.) was adopted. Table 2 shows the polarization observed at 330°, together with the moment computed as $\mu=0{\cdot}012812[(P-R)T]^{\frac{1}{2}}$. Satisfactory agreement with the figures from solutions is displayed, and no abnormal "solvent effect" is indicated.

TABLE 1

OBSERVATIONS ON DIELECTRIC CONSTANTS AND DENSITIES OF ACENAPHTHENE IN CARBON TETRACHLORIDE AND DIOXAN AT 25 °C

In carbon tetrachloride					
$10^5 w_2$	0	480	535	780	1243
ε_{12}	2·2270	2·2345	2·2366	2·2399	2·2470
$(d_4^{25})_{12}$	1·5845	1·5814	1·5799	1·5793	1·5775
		1849	1886		
		2·2522	2·2558		
		1·5723	1·5719		
Whence $\Sigma\Delta\varepsilon/\Sigma w_2=1{\cdot}53_6$, $\Sigma\Delta d/\Sigma w_2=-0{\cdot}6600$					
In dioxan					
$10^5 w_2$	0	1013	1098	1187	2468
ε_{12}	2·2090	—	2·2253	2·2204	2·2277
$(d_4^{25})_{12}$	1·0280	1·0283	1·0287	1·0286	1·0292
		2597			
		2·2310			
		1·0295			
Whence $\Sigma\Delta\varepsilon/\Sigma w_2=0{\cdot}931$, $\Sigma\Delta d/\Sigma w_2=0{\cdot}051$					

TABLE 2

POLARIZATION OF GASEOUS ACENAPHTHENE

Temperature (°C)	x/x'	No. of Observations	P (obs.)	μD
330	13·50	7	58·6	$0{\cdot}8_1$

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THE SELF-RETARDATION OF THE AUTOXIDATION OF BENZALDEHYDE*

By M. F. R. MULCAHY† and I. C. WATT†

The autoxidation of benzaldehyde decelerates more rapidly as the reaction proceeds than can be accounted for by the consumption of the aldehyde (Almquist and Branch 1932; Mulcahy and Watt 1953; see also curve *A* in Fig. 1). Waters and Wickham-Jones (1951) who worked with benzaldehyde containing *p*-cresol, a weak inhibitor, have observed that " changes in the oxygen-uptake rate are associated with changes in the peroxide content of the aldehyde " which rises to a maximum and falls away again during the reaction (Fig. 1, curve *C*). They consider that the oxidation is catalysed by the peroxide (perbenzoic acid) and attribute the decline in rate to the decrease in peroxide concentration [*P*]. However, this does not explain the fact (Bäckström 1927; Almquist and Branch 1932; Mulcahy and Watt loc. cit.) that the rate of oxidation of the pure aldehyde declines from the beginning even though during the initial period the peroxide concentration is increasing (Fig. 1). Self-retardation during this period must be due to the formation of an inhibiting substance, probably as a trace by-product of the main reaction (Almquist and Branch 1932; Mulcahy and Watt loc. cit.). The purpose of this note is to report observations which amplify the statement of Waters and Wickham-Jones quoted above and which indicate that the " auto-inhibitor " is produced either directly or indirectly from perbenzoic acid.

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† Division of Tribophysics, C.S.I.R.O., Melbourne; present address: Chemistry Department, Cornell University, Ithaca, N.Y.

The rate in the presence of a small concentration of inhibitor $[X]$ is given approximately by

$$\rho \approx \frac{\rho_0}{1+C[X]}, \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (1)$$

where ρ_0, the rate in the absence of the inhibitor, and C are constants when, as will be assumed here, the reagent concentrations and the initiation rate are

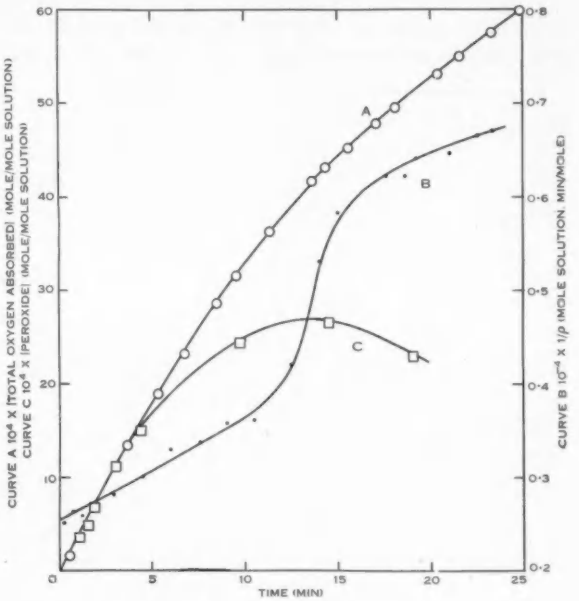

Fig. 1.—Progressive oxidation of benzaldehyde in benzene solution (mole fraction benzaldehyde = 0·224 ; temp. = 31 °C). *A*, total concentration of oxygen absorbed ; *B*, reciprocal of rate of oxygen absorption ; *C*, peroxide concentration.

constant. Since in the present case the inhibitor is produced by the oxidation, $[X]$ will be a function of time. The rate at time t will be

$$\rho \approx \frac{\rho_0}{1+Cf(t)}, \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (2)$$

and consequently

$$\frac{1}{\rho} \approx \frac{1}{\rho_0} + \text{const. } f(t). \quad \ldots\ldots\ldots\ldots\ldots \quad (3)$$

Thus a plot of $1/\rho$ against time will indicate the variation in the relative concentration of the inhibitor during the reaction. Comparison of this variation with that of the concentrations of other products may throw light on the source of the retardation.

Curve *B* in Figure 1 shows that $1/\rho$ increases progressively but not uniformly with *t*. Comparison with the peroxide concentration (curve *C*) shows that the *rate* of increase of $1/\rho$ follows the peroxide concentration, rising to a maximum when the peroxide is at its maximum and falling again as it declines. A similar result is shown in Figure 2 which refers to a solution of benzaldehyde containing initially a trace of retarder. This lowered the overall rate but did not affect the general characteristics of the reaction. However, it did introduce a small degree of irreproducibility in the variation of the rate with time particularly in the later stages of the reaction. For this reason the total oxygen absorption has been chosen as abscissa rather than the time. Figure 3 was plotted in the

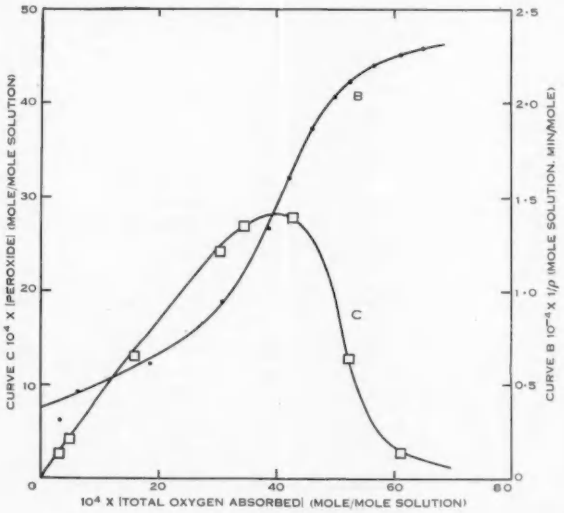

Fig. 2.—Oxidation of benzaldehyde in benzene solution containing a trace of retarder (mole fraction benzaldehyde = 0·224 ; temp. = 31 °C). *B*, peroxide concentration ; *C*, reciprocal of rate.

same way from Almquist and Branch's (loc. cit.) measurements of oxygen absorption by the undiluted aldehyde. Since the total oxygen absorption (i.e. $\int_0^t \rho dt$) increases uniformly with time (though ρ of course does not), the curves shown in Figures 2 and 3 are also indicative of a parallelism between the rate of increase of $1/\rho$ and the peroxide concentration. $1/\rho$ itself is not simply related to the peroxide concentration. This would seem to eliminate the possibility suggested by Raymond (1931) that perbenzoic acid is the inhibitor.

It appears that the inhibitor is produced by decomposition or some other reaction of the peroxide. If this is the case, assuming the reaction to be first order with respect to peroxide, it would follow that

$$\frac{d(1/\rho)}{dt} \propto \frac{d[X]}{dt} \propto [P], \quad \ldots\ldots\ldots\ldots\ldots\ldots (4)$$

and hence that

$$\frac{1}{\rho}=\frac{1}{\rho_0}+\text{const.}\int_0^t [P]dt. \quad \ldots\ldots\ldots\ldots\ldots (5)$$

Figure 4 which is derived from Figure 1 shows that equation (5) is obeyed. In view of the errors involved in evaluating the integral and the approximate nature of equation (1), the closeness of the curve to linearity could be to some extent fortuitous, but it seems sufficiently clear that the peroxide is the source of the inhibitor.

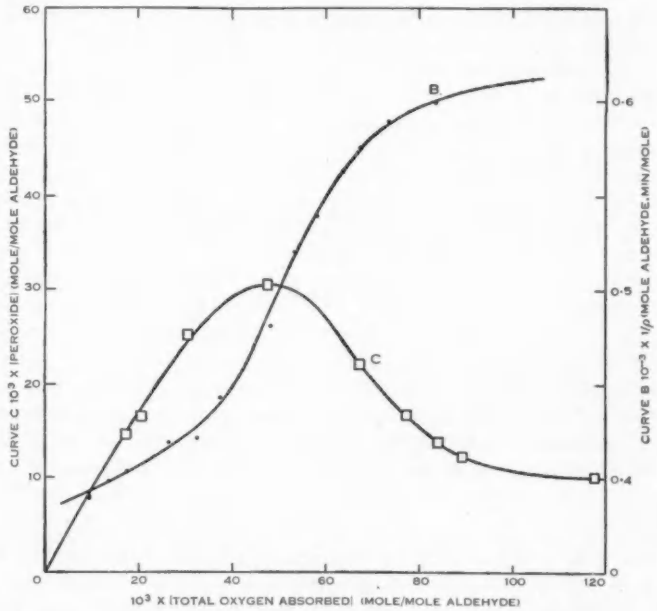

Fig. 3.—Oxidation of benzaldehyde (mole fraction = 1 ; temp. = 25 °C). Results derived from Almquist and Branch (1932). *B*, peroxide concentration ; *C*, reciprocal of rate.

It is emphasized that this work does not show that catalysis by perbenzoic acid is absent ; but it does indicate that the *predominant* effect of changes in the peroxide concentration on the rate arises from the production of inhibitor. To this extent the statement of Waters and Wickham-Jones is applicable to the oxidation of the pure aldehyde. We have found sigmoid $1/\rho$ curves with benzene solutions from 0·1 to 1·0 mole fraction benzaldehyde and also when the reaction is partly initiated by benzoyl peroxide. In the presence of excess benzoic acid, however, the sigmoid character disappears and the initial deceleration is less marked and more uniform (cf. Almquist and Branch 1932 ; Mulcahy and Watt loc. cit.). Since the peroxide concentration in the early stages is lowered and the

pronounced maximum eliminated by benzoic acid (Almquist and Branch loc. cit.) this observation supports the view that the inhibitor is produced from the peroxide.

No serious attempt was made to identify the inhibitor. However, the indophenol and ferric chloride tests when applied after prolonged oxidation both gave faint but definite positive reactions for phenolic compounds. These have been detected previously by Brunner (1927). Such substances, which could be derived from free hydroxyl radicals (Merz and Waters 1949), are well known to be inhibitors.

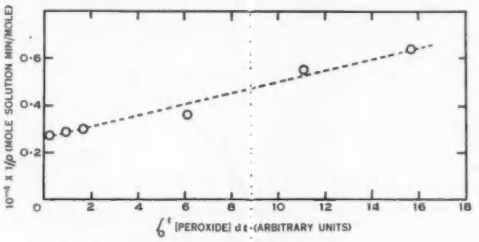

Fig. 4.—Plot of reciprocal of rate against $\int_0^t$ [peroxide]dt.

Experimental

The reagents and experimental technique were as described in a previous publication (Mulcahy and Watt loc. cit.) except that the peroxide estimations recorded in Figure 2 were carried out by a colorimetric method. This was less accurate than the titration method described previously.

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THE STABILITY CONSTANT OF THE TRIS–1,10–PHENANTHROLINE FERROUS ION*

By H. A. McKenzie†

Dwyer and Nyholm (1946) first determined the stability constant of the intensely red coloured tris-1,10-phenanthroline ferrous ion (ferroin). No evidence had been reported for other species involving ferrous ion and phenanthroline. Assuming no interaction between ferric ion and phenanthroline they attributed the change in redox potential of the ferrous-ferric couple caused by the addition of phenanthroline to be due to the formation of the tris complex ferrous ion. The log K_s for the overall stability constant was found to be 17·7. Subsequently Dwyer and McKenzie (1947) determined the constant for the tris-2,2′-dipyridyl ferrous ion by a similar method and obtained a log K_s of $16{\cdot}4 \pm 0{\cdot}5$. At the same time McKenzie (1947) demonstrated that citrate ion interfered markedly in the determination of iron by dipyridyl, but not in the determination of phenanthroline. This work showed that the phenanthroline complex was more stable than the redox results indicated.

Baxendale and George (1950) showed by kinetic and equilibrium measurements that log K_s for the dipyridyl complex was 17·1 in reasonable agreement with the redox determination. However, spectrophotometric and kinetic studies of ferroin by Lee, Kolthoff, and Leussing (1948*a*, 1948*b*) gave a log K_s of 21·3. Brandt, Dwyer, and Gyarfas (1954) presumed that the discrepancy of the ferroin constant based on redox measurements is due to an uncorrected interaction between ferric ion and phenanthroline. This is believed by Smith (1949, personal communication) to be in the form of a yellow-brown complex.

In the present work a redetermination of log K_s for ferroin has been made using the redox method. Care was taken to avoid a large excess of chelate since this shifts the redox potential to the very poorly poised region, with resultant difficulty in obtaining an accurate stable potential. The pH was kept in the region of 1·5, since the work of Harvey and Manning (1952) indicated that at this pH the equilibrium interaction of ferric ion and phenanthroline is negligible. Furthermore, spectrophotometric measurements at 396 and 512 mμ were made using a procedure similar to that of Harvey, Smart, and Amis (1955). These showed that there was no appreciable interaction of ferric ion and phenanthroline under the experimental conditions. The general procedure and conditions of ionic strength were similar to those of Dwyer and McKenzie (1947).

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† Physico-Chemical Laboratory, Division of Food Preservation and Transport, C.S.I.R.O., Biochemistry Department, University of Sydney.

Results and Discussion

In Table 1 are shown the pH of the reaction mixture; ΔE, the shift in redox potential; $(\text{phen H})^+$, the molar concentration of free phenanthrolinium ion; and the log K_s of the overall stability constant of ferroin at 25 °C.

TABLE 1
DETAILS OF REACTION MIXTURE

pH	ΔE (V)	Concentration $(\text{phen H})^+$ (mole/l)	Log K_s
1·44	0·110	0·00205	21·2
1·45	0·0835	0·00109	21·6
1·37	0·135	0·00352	21·1

The mean log K_s value of 21·3 is in agreement with that of Lee, Kolthoff, and Leussing (1948*a*, 1948*b*). Thus under appropriate experimental conditions the redox method gives results for log K_s in accordance with the other methods and is in satisfactory agreement with the observed reactions of iron and phenanthroline.

Grateful acknowledgment is due to Dr. F. P. Dwyer, Chemistry Department, University of Sydney and Professor G. F. Smith, Chemistry Department, University of Illinois for helpful discussions.

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CORRIGENDUM

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Page 453, box heading of 2nd last column of Table 2: *For* $\frac{\beta(d) \text{ calc.}}{2{\cdot}5}$ *read* $\frac{\beta(d) \text{ calc.}}{2{\cdot}5}$.

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